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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

July 31, 1998

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: The HED Chapter of the Reregistration Eligibility Decision Document (RED) for Iprodione (PC Code: 109801, List A Case No. 2335, DP Barcode: D233218).

FROM: Christina Scheltema, Biologist
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Christina Scheltema 7/31/98

THRU: Steve Knizner, Branch Senior Scientist
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for 7/31/98

TO: Dennis Deziel, Chemical Review Manager
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and

Mark Wilhite, Special Review Manager
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Special Review and Reregistration Division (7508W)

Please find attached the Human Health Assessment for the Iprodione Reregistration Eligibility Decision Document (RED) Case No. 2335. This chapter incorporates information from the Toxicology chapter from Linda Taylor (ATTACHMENT I), the Product and Residue Chemistry chapter from John Abbotts (ATTACHMENT II), the Occupational/Residential Exposure Assessment from John Leahy (ATTACHMENT III), and the Dietary Risk Analysis from Brian Steinwand (ATTACHMENT IV). Kelly O'Rourke and Bill Smith also contributed to this document, to the occupational and residential exposure assessment and residue chemistry assessment, respectively.

Required Data:

1. Toxicology Studies

There are no data gaps for the standard Subdivision F Guideline Requirements for a food-use chemical required by 40 CFR Part 158. However, the 1994 RfD Committee recommended a postnatal developmental toxicity study in rats due to the close structural similarity of Iprodione to Vinclozolin and because of the effects seen in the reproductive system of male rats, as well as in the adrenal glands of both sexes of rats, in the combined chronic toxicity/ carcinogenicity study. In response to the above recommendation, the Registrant in 1997 submitted a special study that examined the sex differentiation of offspring from pregnant rats exposed orally to Iprodione (MRID No. 44365001).

The 1998 Hazard Identification Review Committee (HIARC) determined that there are outstanding questions with regard to postnatal exposure that remain to be addressed in light of the observed effects of Iprodione on the testes and its proposed mode of action (disruption of testosterone biosynthesis). Iprodione has been shown to alter anogenital distances in male fetuses following exposure during late gestation and there is evidence of toxicity to the male reproductive organs in chronic studies in rats. Also, no data are available on the effect of Iprodione on sperm count, motility or morphology in rat or other species. Therefore, the HIARC concluded that an assessment of effects on the male reproductive system following pre and/or postnatal exposure is required and these aspects can be addressed by conducting the study as described in OPPTS 870.3800

2. Chemistry Studies

a. Product Chemistry

Data are still required on density of the Technical Grade Active Ingredient (TGAI). Data are required for a new requirement concerning UV/visible absorption for the PAI (OPPTS 830.7050). All other pertinent data requirements are satisfied for the Iprodione 95% T/TGAI. Provided that the registrant submits the data required in the attached data summary table for the 95% T, and either certifies that the suppliers of beginning materials and the manufacturing process for the Iprodione TGAI have not changed since the last comprehensive product chemistry review or submits a complete updated product chemistry data package, HED has no objections to the Reregistration of Iprodione with respect to product chemistry data requirements.

b. Residue Chemistry

Data requirements for rotational crops remain outstanding. HED previously advised that depending on crops and plantback intervals chosen, residues in rotational crops would be expected to increase dietary exposure to Iprodione residues (CBRS 16553, 4/17/96, J. Abbotts). During review of a petition for use on cotton, HED required that rotations be restricted to those crops for which primary Iprodione tolerances were already established (PP 2F04111, CBTS 15214, 8/11/95, N. Dodd). HED recommends that a similar restriction on all Iprodione labels, with obvious exceptions for crops that are not normally rotated, be required.

3. Occupational/Residential Exposure Studies

a. Handler Studies

Data gaps exist for the following scenarios:

- (9) - no chemical specific or Pesticide Handler's Exposure Database (PHED) baseline data exist for applying with a low pressure/high volume handgun to turfgrass.
- (16)- no chemical specific or PHED data exist for mixing/loading/applying as a seed soak treatment.
- (17) - no chemical specific or PHED data exist for mixing/loading/applying as a commercial seed treatment in slurry form.
- (18) - no chemical specific or PHED data exist for mixing/loading/applying solution as a dip treatment.

Labeling Requirements:

To be completed after risk mitigation discussions with the registrant.

Attachments

cc: L. Taylor, John Leahy, B. Steinwand (DRES), C. Scheltema , S. Knizner,
RCAB File, List B File, Subject File
RDI: CS 07/xx/98, SAK 07/xx/98
CM#2: Room 718L: 308-2201: 7509C

TABLE OF CONTENTS

I. EXECUTIVE SUMMARY

Background

The Health Effects Division has evaluated the Iprodione database and determined that the data are adequate to support Reregistration. The toxicological database is adequate to support Reregistration. However, a pre- and postnatal exposure developmental/reproductive toxicity study is required to assess the effects of Iprodione on the developing male reproductive system. These aspects can be addressed by following the new guidelines for reproductive toxicity testing (OPPTS 870.3800). Product chemistry data are still required on density of the TGAI. Data are necessary to satisfy the new requirement concerning UV/visible absorption (OPPTS 830.7050). Residue chemistry Reregistration data requirements remain outstanding for analytical method, confined and field rotational crops, and residues in water from use on rice.
There are data gaps for occupational and residential exposure studies. Some use scenarios can not be evaluated for Reregistration until data are submitted to support these uses.

Iprodione is a contact and/or locally systemic fungicide. It is registered for use on a variety of field, fruit, and vegetable crops. Some Iprodione products are registered for homeowner use on turf and in home vegetable gardens. Iprodione is available in the following formulations: technical (95 percent active ingredient), liquid soluble concentrate (14 and 41.6 percent active ingredient), wettable powder (33.3 and 50 percent active ingredient), a dry flowable (50 percent active ingredient), flowable concentrate (41.6 percent active ingredient), emulsifiable concentrate (19.65, 23.3 and 50 percent active ingredient), and as a granular (1.02 and 1.3 percent active ingredient). Some wettable powder formulations are contained in water-soluble packaging.

Hazard

Iprodione is associated with toxicity of the liver, adrenals, and male and female reproductive organs in animal studies. The proposed mode of action of Iprodione is disruption of testosterone biosynthesis. Iprodione is also associated with tumors of these organ systems. Iprodione has been classified as a B2 carcinogen by the OPP Cancer Assessment Committee. The Committee determined that it is appropriate to quantify cancer dose response using the linearized low dose extrapolation model (Q_1* approach). Leydig cell tumors were chosen for human health risk assessment as the most sensitive endpoint. Iprodione was negative for induction of gene mutations, in a sister chromatid exchange assay, and for in vitro chromosomal aberration in the presence and absence of metabolic activation. There was no evidence of clastogenic or aneugenic effects at any dose or harvest time from an in vivo mouse micronucleus assay. The prenatal developmental toxicity study in rabbits, the special prenatal study in rats, and the two-generation reproduction study in rats demonstrated no indication of increased susceptibility to *in utero* and/or postnatal exposure to Iprodione. Based on the weight-of-the-evidence of all available studies, the Hazard Identification Assessment Review Committee (HIARC) concluded that there was no increased susceptibility to rat and rabbit fetuses following *in utero* and/or post

natal exposure to Iprodione. In 3 out of 4 studies examined, maternal or parental no observed effect levels (NOELs) are lower or equivalent to the offspring NOELs. In the fourth study, the results were inconclusive regarding maternal versus offspring toxicity. The FQPA Safety Factor Assessment Review Committee determined that **the additional 10x Safety Factor** for enhanced sensitivity to infants and children (as required by FQPA) **should be reduced to 3x for the following reasons:**

1) No enhanced susceptibility was seen in rat and rabbit developmental and the two generation reproduction study in rats. 2) The critical endpoint for acute dietary risk assesssment (decreased AGD) was seen at a high dose (120 mg/kg/day) and there were only marginal differences in the degree of decreased AGD between the doses 20 mg/kg/day (2.44), 120 mg/kg/day (2.32) and 250 mg/kg/day (2.10) thus indicating the "true" NOEL could be higher than the one established at 20 mg/kg/day. 3) The proposed mode of action of Iprodione is disruption of testosterone biosynthesis. 4) The use of a realistic dietary exposure data (refined using monitoring data and percent crop treated). 5) The endpoints selected for both the acute (AGD) and the chronic (histopathology of male reproductive system) risk assessments are based on developmental/reproductive effects. 6) The uncertainty with regard to the pre/post natal exposure study requested by the HIARC which may confirm the effects seen in the standard developmental/reproductive studies.

A general metabolic pathway for Iprodione in the rat indicates that biotransformation results in hydroxylation of the aromatic ring, degradation of the isopropylcarbamoyl chain, and rearrangement followed by cleavage of the hydantoin moiety. Additionally, structural isomers of Iprodione resulting from molecular rearrangement, as well as intermediates in the pathway, were detected.

Five aggregate exposure and risk assessments were conducted for Iprodione. These risk assessments reflect non-occupational exposures and include combined exposures to Iprodione through food and water in the diet, and through homeowner uses. They are: acute dietary (includes 1-day, high-end exposures through food and water only), chronic dietary (includes long-term exposures to average residues in food and water only, because there are no chronic residential exposure scenarios), cancer (includes average exposures through food, water, and residential uses), and short- and intermediate-term risk assessments (includes exposures of several days to a few months through food, water and through residential uses). These five risk assessments capture exposure estimates for the general public through dietary (food and water) and residential exposures. Risk assessments for occupational exposures were separated into applicator/handler and post-application exposure scenarios. The applicator/handler exposure scenarios include risk assessments for short- and intermediate-term inhalation exposures, and a combined dermal and inhalation cancer risk assessment for long-term exposures. Chronic (non-cancer) and cancer risk assessments for post-application workers are included.

For the **acute dietary** exposure and risk assessment, the toxic endpoint selected for risk assessment was the no observed effect level (NOEL) of 20 mg/kg/day based on decreased

anogenital distance (AGD) in male offspring observed in the developmental study in rats, in which the lowest observed effect level (LOEL) was 120 mg/kg/day. This was a special study designed to determine the impact of Iprodione on sexual differentiation. The acute dietary risk assessment is only appropriate for females (13 years old or more). An acute toxicological endpoint for the general population was not identified. The uncertainty factor used in this assessment was 300 (100X for intra- and inter-species variability and 3X for FQPA considerations). The resultant acute FQPA RfD for use in the acute dietary risk assessment is 0.06 mg/kg/day.

For the **chronic dietary** exposure and risk assessment, the toxic endpoint selected for risk assessment was the NOEL of 6.1 mg/kg/day based on histopathological lesions in the male reproductive system and the adrenal glands in both sexes at the LOEL of 12.4 (males) and 16.5 (females) mg/kg/day observed in the combined chronic toxicity/carcinogenicity study in rats. The uncertainty factor used in this assessment was 100X for intra- and inter-species variability, giving a Chronic RfD of 0.06 mg/kg/day. The OPP Division Directors recommended the use of an additional 3X uncertainty factor for FQPA considerations. The resultant chronic FQPA RfD is 0.02 mg/kg/day.

For **carcinogenic dietary** risk assessments, a Q_1^* of 4.39×10^{-2} mg/kg/day^{-1} based on Leydig cell tumor formation in male rats was selected for all dietary cancer risk assessments.

Short- and intermediate-term risk assessments are conducted for occupational and residential exposure scenarios associated with a pesticide's use pattern. There is no evidence of **dermal** toxicity during short- and intermediate-term exposures to Iprodione, and the percent absorption of Iprodione through the skin is low (5%). For these reasons, no short- or intermediate-term risk assessments for dermal exposures to Iprodione were required, and these risk assessments have not been conducted. Risk assessments based on short- and intermediate-term exposure to Iprodione through **inhalation** have been conducted. Short- and intermediate inhalation exposures were identified as the handler (mixer/loader/applicator) is exposed to dusts and sprays during handling. The toxic endpoint selected for the short-term risk assessment was based on the developmental study in rats (NOEL of 20 mg/kg/day). An inhalation absorption factor of 100% was applied to the NOEL selected for the short-term assessment, resulting in an equivalent oral dose endpoint for use in short-term inhalation risk assessments of 20 mg/kg/day. For intermediate-term inhalation exposure, the endpoint selected was a NOEL (6.1 mg/kg/day) based on histopathological lesions in the male reproductive system and the adrenal glands in both sexes from the chronic toxicity/carcinogenicity study in rats. An inhalation absorption factor of 100% was used in the assessment resulting in an equivalent oral dose endpoint for use in intermediate-term inhalation risk assessment of 6.1 mg/kg/day. An uncertainty factor of 100 was used for all of the short- and intermediate-term occupational exposure assessments. An uncertainty factor of 300 was used for short- and intermediate-term residential exposure assessments to account for potential exposures of children through home use and associated developmental effects. A long-term inhalation exposure scenario was not identified for Iprodione.

Dermal exposure (long-term) to Iprodione has been identified for occupational and residential risk assessments. For occupational risk assessments, post-application chronic exposure scenarios exist, and for these chronic (non-cancer) risk assessments the NOEL from the chronic/carcinogenicity study in rats (6.1 mg/kg/day) has been selected along with an uncertainty factor of 100, and a dermal absorption rate of 5%. Chronic exposure scenarios were not identified for homeowner uses. For occupational and residential carcinogenic risk assessment, the Q_1* selected for estimates of 4.39×10^{-2} mg/kg/day^{-1}, based on Leydig cell tumor formation in male rats was chosen.

Dietary Exposure and Risk: Food and Water

The main route of exposure to Iprodione for the general public (non-occupational exposures) is through food and registered home owner uses. The **acute dietary risk estimate for females (13+) exceeds HED's level of concern.** This risk estimate is associated with the consumption of Iprodione residues representing the high-end of exposure in food (tolerance level residues without the use of percent crop-treated information) exceed HED's level of concern for females (13+), the only population for which an acute dietary endpoint was determined. The tolerances for stone fruits, berries, and small fruit commodities range from 15 to 25 ppm (40 CFR 180.399). These commodities are likely to be driving the acute dietary risk estimate for females (13+). Probabilistic acute dietary exposure and risk assessments were submitted, reviewed and deemed acceptable. The probabilistic assessment was highly refined using a distribution of residue values for commodities and percent crop-treated data. However, the original analysis submitted used a different toxicological endpoint, a NOEL of 90 mg/kg/day from a rat teratology study, whereas HED's assessments use a NOEL of 20 mg/kg/day from a sexual differentiation study. HED recalculated the probabilistic risk based on the NOEL for sexual differentiation (20 mg/kg/day). The recalculation of the risk estimate resulted in an MOE of 139 at the 99.9th percentile of exposure, which exceeds HED's level of concern (a MOE of 300 is required for this risk assessment). However, as noted above, there is some uncertainty regarding the NOEL of 20 mg/kg/day. There were only marginal differences in the degree of decreased anogenital distance (AGD) between the doses 20 mg/kg/day (2.44), 120 mg/kg/day (2.32) and 250 mg/kg/day (2.10) thus indicating the "true" NOEL could be higher than the one established at 20 mg/kg/day. Because acute dietary risk estimates from exposure to Iprodione in food alone exceed HED's level of concern, any exposure through drinking water would only contribute more to an already unacceptable risk estimate from food, and result in an unacceptable aggregate acute dietary risk estimate.

The **chronic dietary risk estimate does not exceed HED's level of concern.** This risk estimate is associated with currently registered uses of Iprodione represents **less than or equal to 1% of the chronic RfD** for most subpopulations, and **1.6% of the chronic RfD for Non-Nursing Infants (< 1 year old) the most highly exposed subpopulation.** The chronic analysis for Iprodione is a highly refined risk estimate of dietary exposure using the most recent percent crop treated data (1995) and anticipated residue data from monitoring programs (USDA's PDP) and field trials. Based on the risk estimates calculated in this analysis, it appears that chronic dietary

risk from the uses recommended through Reregistration, is not of concern. OPP does not expect exposure to Iprodione through drinking water to impact the chronic dietary risk assessment significantly.

The upper bound dietary cancer risk estimate (6.5×10^{-6}) exceeds HED's level of concern. This risk estimate was based on a refined estimate of dietary exposure using the most recent percent crop-treated data (1995) and anticipated residue data from monitoring programs (USDA's PDP) and field trials (as described above for the chronic dietary risk estimate). The calculated risk estimate is above the range the Agency generally considers negligible for excess life time cancer risk (1×10^{-6}). The commodities which contribute the most to this risk figure are grapes (including wine and sherry) at 3.0×10^{-6}, stone fruits at 1.5×10^{-6}, and small fruits and berries at 1.0×10^{-6}. Because carcinogenic dietary risk estimates from exposure to Iprodione in food alone exceed HED's level of concern, any exposure through drinking water would only contribute more to an already unacceptable risk estimate from food and result in an unacceptable aggregate cancer dietary risk estimate.

Iprodione uses are not expected to impact ground water. Exposure to Iprodione in surface water used potentially as drinking water is indeterminate at this point. Screening models used to provide conservative estimates of upper bound concentrations of Iprodione in surface water indicate that low levels of Iprodione (a few ppb) could be present in surface waters. Of particular concern is the direct aquatic use on rice. This would be the most likely source of Iprodione residues in surface waters.

Contributions to Dietary Risk from 3,5-Dichloroaniline (3,5-DCA)

The cumulative carcinogenic risk estimate for consumption of food and wine containing residues of 3,5-DCA as a result of use of Iprodione, Vinclozolin, and procymidone is 1.3×10^{-6}. This can be considered to be an over-estimate. Metabolism studies for Iprodione and Vinclozolin were used to estimate the amount of 3,5-DCA present in various commodities by using Total Radioactive Residues (TRRs) to convert Iprodione or Vinclozolin exposures to 3,5-DCA exposures. There is another uncertainty in the risk estimate in that a surrogate Q_1^* is being used for 3,5-DCA. However, due to the structural similarities of 3,5-DCA and PCA (parachloroaniline), HED believes that for 3,5-DCA, the use of the PCA Q_1^* represents an upper-bound estimate. These are the best risk estimates that can be supplied by HED.

Because drinking water data on DCA residues in water are not available, HED compared the conservative screening-level model estimates of Iprodione concentrations in surface water to drinking water levels of concern (DWLOCs) for DCA. Because the cancer risk estimate for 3,5-DCA derived from food and wine is 1.3×10^{-6}, the $DWLOC_{cancer}$ is effectively zero (0). Conservative estimates from screening-level models indicate concentrations of 3,5-DCA of 0.4 to 0.5 ppb in surface waters.

Occupational Exposure and Risk: Handler and Post-Application

Occupational exposure to Iprodione residues can occur to pesticide handlers during mixing, loading, and applying Iprodione, and to post-application workers during harvesting activities. For pesticide handlers, risks associated with short- and intermediate-term exposures, and cancer were estimated. Short- and intermediate-term exposures occur through inhalation of dusts and sprays during mixing, loading, and application. Once the dusts and sprays settle shortly after application, the potential for long-term exposures through dermal contact is low for the handler. Since long-term exposures to Iprodione are not expected to occur for handlers, risks associated with chronic, non-cancer effects were not estimated. Cancer risk estimates for handlers were calculated based on the Q* for Leydig cell tumors. The Q_1* approach to calculating cancer risk assumes that any amount of exposure will lead to some degree of risk. For pesticide handlers, exposure of a short duration (1 to 7 days) and intermediate duration (7 days to several months) result in risk estimates that are below HED's level of concern (MOE $\geq$ 100) after maximum mitigation measures have been applied. Cancer risk estimates for handlers result in 3 exposure scenarios with risk estimates > 10^{-4}. However, these risks fall to within the 10^{-4} to 10^{-6} range with mitigation, i.e., added protective clothing or reduced application rates. For exposure scenarios where engineering controls are applicable, all risk estimates are in the range of 10^{-4} to 10^{-6} or below.

For post-application workers, no short- or intermediate-term exposure scenarios were identified, because once sprays and dusts settle, post-application inhalation exposure is not expected to be significant. Therefore, only post-application chronic (non-cancer) and cancer risk have been assessed. Exposure scenarios were identified that warrant chronic (non-cancer) and cancer risk estimates. Chronic risk estimates were based on long-term dermal exposure (defined as $\geq$ 180 days/year) and a NOEL of 6.1 mg/kg/day. Three post-application activities were identified with potential for chronic exposure: golf course maintenance, harvesting small fruits and vegetables, and transplanting, pruning, and bundling of ornamentals. MOEs (chronic risk estimates) for these activities were greater than 100 for all activities depending on the reentry interval. For golf course maintenance and harvesting small fruits and vegetables, acceptable MOEs (100) were achieved zero (0) days after treatment. For activities associated with ornamentals, an acceptable MOE (100) is achieved 4 days after treatment. Cancer risk estimates for post-application workers were based on the Q_1* for Leydig cell tumors and result in risks greater than 10^{-4} for 5 crop type/activity groupings: grape, almond, stone fruit, small fruit and vegetable harvesting, and ornamental activities. These risk estimates were based on surrogate data from HED's PHED. Assumptions from HED's Standard Operating Procedures for Residential Exposure Assessments (residential SOPs) were also used in calculating dislodgeable foliar residues.

Exposure to Iprodione can lead to skin illness requiring medical care. Incident data indicate that skin rashes have been reported in field workers exposed to residues of Iprodione. A few cases (8) have reported relatively minor systemic symptoms such as headache, nausea, and dizziness. Three of the eight cases were reportedly due to field reentry. However, in none of the systemic cases was the exposure considered a probable or definite cause of the effects. Data from

California support the need for reentry intervals to prevent fieldworkers returning to fields immediately after application. Protective clothing to avoid skin rash is warranted for workers handling Iprodione (e.g., applicators and mixer/loaders).

Residential Exposure and Risk: Handler and Post-Application

Residential exposure scenarios were identified for homeowners using Iprodione products. Short- and intermediate-term inhalation risks, and total cancer risks were assessed for homeowners (adults only) handling and applying Iprodione. It is assumed that children and infants are not exposed during outdoor application. There are no indoor uses. Baseline protection and maximum application rates were assumed, and risks were estimated using the residential SOPs. Risks associated with short- and intermediate-term exposure through inhalation for homeowners handling and applying Iprodione products were estimated using the same calculations as used in estimating exposure, dose, and risk for occupational workers handling and applying Iprodione. The calculations for short- and intermediate-term inhalation risks for homeowners handling Iprodione products indicate that the MOEs are greater than 100 using baseline protective clothing for all exposure scenarios considered. Cancer risk estimates for homeowner exposure to Iprodione were calculated based on the same Q* for Leydig cell tumor as all previous cancer risk assessments. Cancer risks for homeowner handlers applying Iprodione are greater than 10^{-6} for the use of: low pressure hand wands on turf and small fruits and vegetables, backpack sprayers on turf, garden hose-end sprayers on all sites except trees, belly grinders for broadcast turf treatments, and granular formulations applied by hand for spot treatments of turf. No chronic exposure scenarios for residential uses of Iprodione were identified; therefore, no chronic (non-cancer) risks were estimated.

Post-application residential exposures have been assessed for cancer risk for adults only. As explained above for occupational post-application exposures, once sprays and dusts settle, post-application inhalation exposure is not expected to be significant. Therefore, risk estimates based on short- and intermediate-term inhalation exposures were not warranted. Also, no chronic exposure scenarios were identified for residential post-application activities. Although chronic exposure scenarios were identified for post-application workers, these same activities for the homeowner are expected to be intermittent and not result in long-term exposures. The post-application exposure assessment for estimating cancer risk was based on the residential SOPs to determine potential risks for the representative scenarios. No Iprodione-specific reentry or transferable residue data were submitted. As in cancer risk estimates for occupational scenarios, estimates for homeowner exposure to Iprodione were calculated based on the same Q* for Leydig cell tumors, and the Q_1* approach to calculating cancer risk assumes that any amount of exposure will lead to some degree of risk. All residential post-application exposure scenarios have cancer risk estimates greater than 10^{-6}. This includes harvesting activities associated with small fruits and vegetables, specifically grapes, and transplanting, pruning and bundling activities associated with ornamentals.

Aggregate Risk Assessments:

Acute Aggregate Risk:
Acute aggregate risk estimates exceed HED's level of concern. The aggregate acute dietary risk estimate includes exposure to Iprodione residues in food and water. However, HED notes that this refined (probabilistic) estimate of exposure to Iprodione residues in food alone exceed HED's levels of concern for acute dietary risk for females 13+ years old. At this point in time and until the exposure to Iprodione in the diet is reduced or a more refined acceptable risk assessment is provided, any additional exposure to Iprodione through drinking water would only cause acute risk estimates to further exceed HED's level of concern. In effect, the drinking water level of concern (DWLOC) for acute effects of Iprodione is zero (0). Although Iprodione uses are not expected impact ground water (available monitoring data show levels at or below limits of quantification and detection), upper bound estimates of Iprodione in surface waters from conservative screening models indicate concentrations of a few parts per billion.

Chronic (Non-Cancer) Aggregate Risk:
Chronic (non-cancer) aggregate risk estimates do not exceed HED's level of concern. The chronic aggregate risk assessment for Iprodione includes risk estimates associated with dietary exposure through food, water, and registered residential uses. No chronic residential use scenarios were identified. Therefore, residential use does not contribute to chronic aggregate exposure to Iprodione. Exposure to Iprodione through food (based on anticipated residues and percent crop-treated data for commodities with published tolerances) represents 1.6% of the chronic RfD for the most exposed subpopulation in the U.S. (non-nursing infants , <1 year old). Exposure to all other groups represents less than or equal to 1% of the chronic RfD.

HED has calculated drinking water levels of concern (DWLOCs) for chronic exposure to Iprodione from commodities with published tolerances in drinking water for the following four subpopulations: the general U.S. population/Hispanics (690 ppb), females, 13-19 years old (590 ppb), and non-nursing infants, <1 year old (197 ppb). These subpopulations were selected because they contain the individuals believed to be those most highly exposed subpopulations representing males, females, and children and infants, respectively. A conservative estimate (tier 1) of average concentrations of Iprodione in surface water is 1 to 3 ppb. The estimated average concentration of Iprodione in surface water is less than HED's levels of concern for exposure to Iprodione in drinking water as a contribution to chronic aggregate exposure. Estimated average concentrations of Iprodione in ground water were not available for comparison against DWLOC values; however, based on Iprodione's physical/chemical characteristics and available, but limited monitoring data, it is not expected to impact ground water significantly.

Therefore, based on the available information, HED concludes with reasonable certainty that residues of Iprodione in drinking water (when considered along with exposure from food uses) would not result in an unacceptable chronic aggregate human health risk estimate at this time. HED bases this determination on a comparison of estimated concentrations of Iprodione in surface water to back-calculated "levels of concern" for Iprodione in drinking water. The

estimate of Iprodione in surface water is derived from a water quality model that uses conservative assumptions (health-protective) regarding the pesticide transport from the point of application to surface water. Because HED considers the aggregate risk resulting from multiple exposure pathways associated with a pesticide's uses, levels of concern in drinking water may vary as those uses change. If new uses are added in the future, HED will reassess the potential impacts of Iprodione on drinking water as a part of the aggregate risk assessment process.

If concentration estimates of Iprodione in ground water become available, they should be compared to the aforementioned DWLOC values to determine if the estimates exceed the DWLOC values.

Cancer Aggregate Risk:

Combined exposure and risk estimates for each of the residential exposure scenarios plus dietary exposure to Iprodione residues results in cancer risk estimates that are all greater than 10^{-6}. Because individual cancer risk estimates for exposures to Iprodione residues through food and residential uses each exceed HED's level of concern individually, combined exposures through these routes result in an aggregate risk that further exceeds HED's level of concern. Any additional exposure through water would cause the risk estimate to further exceed HED's level of concern. Effectively, the DWLOC for cancer is zero (0). Individual risks associated with dietary exposure and residential exposures must be reduced before additional exposure through drinking water would be acceptable. The dietary (food) cancer risk estimate has been highly refined. The residential risk estimates were derived using the Residential SOPs and could be further refined if chemical specific data for residential exposure scenarios are supplied.

Short-term Aggregate Risk:

Short-term aggregate risk estimates do not exceed HED's level of concern. Aggregate risk estimates associated with short-term risk include exposures to average residues of Iprodione in the diet (food and water) and inhalation exposure (1 to 7 days in duration) through the residential application of Iprodione. The default assumptions used in this aggregate risk estimate are that the homeowner's inhalation exposure to Iprodione is equivalent to an oral exposure (100% absorption of the inhaled residues). Dietary exposures (average residues for food) for the aggregate assessment were obtained from the chronic DRES analysis. The toxic endpoint selected for the short-term risk assessment for exposures to Iprodione through inhalation is the acute oral endpoint also selected for the acute dietary risk assessment, i.e., the acute FQPA RfD. Therefore, the aggregate short-term risk assessment was based on the acute FQPA RfD. The uncertainty factor for both the acute dietary and the short-term inhalation risk assessments is 300. The aggregate risk assessment includes exposures to average concentrations of Iprodione residues in the diet from commodities with existing tolerances, and the high-end exposure scenario associated with homeowners applying Iprodione with a belly grinder to a lawn. The resulting risk estimate represents 3.6% of the acute FQPA RfD for the U.S. population representing the most exposed population of adult males and females. It is assumed that children and infants do not apply pesticides. Although average residues of Iprodione in drinking water were not available, DWLOCs for this short-term aggregate risk assessment were calculated.

They were: for the U.S. population (2000 ppb), and for females representing women 13+ years of age and nursing (1700 ppb). Based on the available information on Iprodione's impact on surface and ground water, HED believes that Iprodione's impact on drinking water will not affect the aggregate short-term risk significantly. Therefore, HED concludes with reasonable certainty that residues of Iprodione in drinking water (when considered along with exposure from food and residential uses) would not result in an unacceptable short-term aggregate human health risk estimate at this time. Any change in use pattern would necessitate a reassessment of Iprodione risk estimates.

Intermediate-term Aggregate Risk:

Intermediate-term aggregate risk estimates do not exceed HED's level of concern. Aggregate risk estimates associated with intermediate-term risk includes exposures to average residues of Iprodione in the diet (food and water) and inhalation exposure (7 days to several months in duration) through the residential application of Iprodione. The default assumptions used in this aggregate risk estimate are that the homeowner's inhalation exposure to Iprodione is equivalent to an oral exposure (100% absorption of the inhaled residues). Dietary exposures (average residues for food) for the aggregate assessment were obtained from the chronic DRES analysis. The toxic endpoint selected for the intermediate-term risk assessment for exposures to Iprodione through inhalation is the chronic oral endpoint also selected for the chronic dietary risk assessment, i.e., the chronic RfD. Therefore, the aggregate intermediate-term risk assessment was based on the chronic RfD. The uncertainty factor for both the chronic dietary and the intermediate-term inhalation risk assessments is 300. The aggregate risk assessment includes exposures to average concentrations of Iprodione residues in the diet from commodities with existing tolerances, and the high-end exposure scenario associated with homeowners applying Iprodione with a belly grinder to a lawn. The resulting risk represents 9.5% of the chronic RfD for the U.S. population representing the most exposed population of adult males and females. It is assumed that children and infants do not apply pesticides. Although average residues of Iprodione in drinking water were not available, DWLOCs for this intermediate-term aggregate risk assessment were calculated. They were: for the U.S. population (600 ppb), and for females representing women 13+ years of age and nursing (540 ppb). Based on the available information on Iprodione's impact on surface and ground water, HED believes that Iprodione's impact on drinking water will not affect the aggregate intermediate-term risk significantly. Therefore, HED concludes with reasonable certainty that residues of Iprodione in drinking water (when considered along with exposure from food and residential uses) would not result in an unacceptable intermediate-term aggregate human health risk estimate at this time. Any change in use pattern would necessitate a reassessment of Iprodione risk estimates.

Conclusion

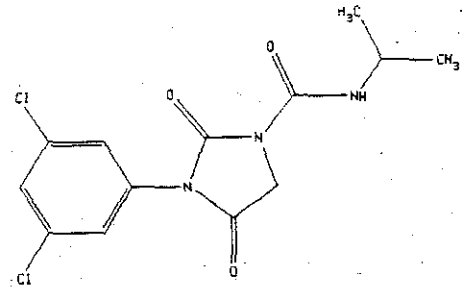
In conclusion, according to the exposure and risk assessments described here, currently registered uses of Iprodione result in dietary risk estimates for acute exposures through food alone that exceed HED's level of concern. Any additional acute exposure through drinking water would worsen an already unacceptable risk estimate. Risk estimates for chronic exposures through food

and water (there are no chronic exposure scenarios for residential uses) do not exceed HED's level of concern. Cancer risk estimates for exposures through food and residential uses each exceed HED's level of concern, individually. Any additional exposure through drinking water would worsen an already unacceptable cancer risk estimate. Risks associated with short- and intermediate-term exposures through food, water and residential uses do not exceed HED's level of concern. Dietary exposure to 3,5-dichloroaniline (DCA) in food and wine and drinking water through uses of Iprodione contributes to estimates of dietary cancer risk. Occupational risk estimates associated with application, mixing, loading and reentry activities do not exceed HED's of concern for exposures of a short duration (1 to 7 days) and intermediate duration (7 days to several months); all short- and intermediate-term inhalation risk estimates are below HED's level of concern (MOE $\geq$ 100) after maximum mitigation measures have been applied. Cancer risk estimates for pesticide handlers result in 3 exposure scenarios with risk estimates > 10^{-4}. However, these risks fall to within the 10^{-4} to 10^{-6} range with mitigation, i.e., added protective clothing or reduced application rates. For exposure scenarios where engineering controls are applicable, all risk estimates are in the range of 10^{-4} to 10^{-6} or below. Cancer risk estimates for post-application workers result in risks greater than 10^{-4} for 5 crop type/activity groupings: grape, almond, stone fruit, small fruit and vegetable harvesting, and ornamental activities.

II. SCIENCE ASSESSMENT

A. Physical and Chemical Properties Assessment

Iprodione [3-(3.5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide] is a contact and/or locally systemic fungicide registered for use on a variety of field, fruit, and vegetable crops.



Empirical Formula:	$C_{13}H_{13}Cl_2N_3O_3$
Molecular Weight:	330.17
CAS Registry No.:	36734-19-7
Shaughnessy No.:	109801

1. Identification of Active Ingredient

Iprodione is a white odorless crystalline solid with a melting point of ~128 C. Iprodione is soluble in dichloromethane (45 g/100 mL), acetone (34 g/100 mL), ethyl acetate (23 g/100 mL), acetonitrile (17 g/100 mL), and toluene (15 g/100 mL), but is practically insoluble in water (13 mg/L). Iprodione is stable under normal storage conditions.

2. Manufacturing Use Products

A search of the Reference Files System (REFS) conducted 12/11/96 identified two Iprodione manufacturing-use products (MPs) registered under Shaughnessy No. 109801: the Rhone-Poulenc Ag Company 95% T and 50% FI (EPA Reg. Nos. 264-452 and 264-558, respectively). Because Iprodione is a List B chemical, only the 95% T/TGAI is subject to a Reregistration eligibility decision.

3. Regulatory Background

The Iprodione Phase 4 Review dated 3/15/91 by C. Olinger required additional generic and product-specific product chemistry data for the Rhone-Poulenc 95% T/TGAI. Data submitted concerning GLNs 63-7 and 63-9 (OPPTS 830.7300 and 830.7950) were found to be adequate for Phase 5 review; Rhone-Poulenc committed to conduct new studies concerning the remaining guideline requirements.

Adequate data concerning the potential for formation of polyhalogenated dibenzo-p-dioxins and/or polyhalogenated dibenzofurans during the manufacture of Iprodione have been submitted. CBRS has concluded that reaction conditions are not favorable to dioxin/dibenzofuran formation, and that trichlorophenols (TCDD precursor), tetrachlorophenols, or other highly chlorinated impurities, are not probable impurities.

The current status of the product chemistry data requirements for the Iprodione technical product is presented in the attached data summary table. Refer to this table for a listing of the outstanding product chemistry data requirements.

4. Conclusions

Data are still required on density of the TGAI. Data are required for a new requirement concerning UV/visible absorption for the PAI (OPPTS 830.7050). All other pertinent data requirements are satisfied for the Iprodione 95% T/TGAI. Provided that the registrant submits the data required in the attached data summary table for the 95% T, and either certifies that the suppliers of beginning materials and the manufacturing process for the Iprodione TGAI have not changed since the last comprehensive product chemistry review or submits a complete updated product chemistry data package, CBRS has no objections to the Reregistration of Iprodione with respect to product chemistry data requirements.

The Iprodione Phase 4 Review dated 3/15/91 by C. Olinger required additional generic and product-specific product chemistry data for the Rhone-Poulenc 95% T/TGAI. Data submitted concerning GLNs 63-7 and 63-9 (OPPTS 830.7300 and 830.7950) were found to be adequate for Phase 5 review; Rhone-Poulenc committed to conduct new studies concerning the remaining guideline requirements.

Adequate data concerning the potential for formation of polyhalogenated dibenzo-p-dioxins and/or polyhalogenated dibenzofurans during the manufacture of Iprodione have been submitted. CBRS has concluded that reaction conditions are not favorable to dioxin/dibenzofuran formation, and that trichlorophenols (TCDD precursor), tetrachlorophenols, or other highly chlorinated impurities, are not probable impurities.

The current status of the product chemistry data requirements for the Iprodione technical product is presented in the attached data summary table. Refer to this table for a listing of the outstanding product chemistry data requirements.

B. Human Risk Assessment

1. Hazard Assessment

a. Toxicology Database

The toxicology database on Iprodione is not complete but is adequate to support a Reregistration eligibility decision. The Reregistration toxicology profile for Iprodione is summarized in the Appendix, in Table 1.

b.Acute Toxicity

Sufficient data are available on the acute toxicity of Iprodione. Iprodione is not acutely toxic via the oral, dermal, inhalation, or ocular routes of exposure. Acute toxicity values and categories for technical are summarized in Table 1.

TABLE 1. Acute Toxicity of technical Iprodione.

Guideline	**Study Type**	**MRID #**	**Results**	**Toxicity Category**
81-1	Acute Oral - rat	42306301	LD_{50} = 4468 mg/kg	III
81-2	Acute Dermal - rabbit	40567601	LD_{50} > 2000 mg/kg	III
81-3	Acute Inhalation - rat	42946101	LC_{50} = > 5.16 mg/L	IV
81-4	Primary Eye Irritation - rabbit	41867301	mild irritant	III
81-5	Primary Skin Irritation - rabbit	41867302	not an irritant	IV
81-6	Dermal Sensitization - guinea pig	40567602 42524601	not a dermal sensitizer	-

In an acute oral toxicity study with rats, the LD_{50} was 4468 mg/kg, which is toxicity category III [Guideline 81-1; MRID 42306301]. The LD_{50} in an acute dermal toxicity study with rabbits was found to be greater than 2000 mg/kg. This is toxicity category III [Guideline 81-2; MRID 40567601]. In an acute inhalation toxicity study with rats, the LC_{50} was greater than 5.16 mg/L for 4 hours. This is toxicity category IV [Guideline 81-3; MRID 42946101].

In a primary eye irritation study with rabbits, Iprodione was a mild ocular irritant. This is toxicity category III [Guideline 81-4; MRID 41867301]. Iprodione did not induce irritation in a primary dermal irritation study in rabbits. This is toxicity category IV [Guideline 81-5; MRID 41867302].

In a dermal sensitization study in guinea pigs, Iprodione was not found to be a dermal sensitizer [Guideline 81-6; MRID 40567602, 42524601].

c. Subchronic Toxicity

Sufficient data are available on the subchronic toxicity of Iprodione. In a 21-day dermal toxicity study, five New Zealand rabbits/sex/group were administered Iprodione [96.2%] via the skin at dose levels of 0, 100, 500, and 1000 mg/kg/day for 21 days. There were no deaths or clinical signs of toxicity, and no adverse effects were observed on body weight, food consumption, the skin, liver, or kidneys. **The NOEL is 1000 mg/kg/day, the highest dose tested** [Guideline §82-2; MRID 42023201].

In a subchronic feeding study, 10 Crl:CD(SD)BR rats/sex/group were administered Iprodione [95.7%] via the diet at dose levels of 0, 1000 ppm [♂♂ 78/♀♀ 89 mg/kg/day], 2000 ppm [♂♂ 151/♀♀ 189 mg/kg/day], 3000 ppm [♂♂ 252/♀♀ 266 mg/kg/day], and 5000 ppm [♂♂ 355/♀♀ 408 mg/kg/day] for 90 days. Signs of toxicity included hunched posture, pilo-erection, pale and/or cold extremities, an emaciated appearance, decreased body weight [♂♂ 75%, 52%, and 39% of control/♀♀ 86%, 70%, and 55% of control at the 2000, 3000, and 5000 ppm dose levels, respectively], decreased body-weight gain [♂♂ 61% and 26% of control/♀♀ 70% and 38% of control at the 2000 and 3000 ppm dose levels, respectively], negative body-weight gain for both sexes at 5000 ppm, decreased food consumption [81% of control for 2000 ppm males; 69%/79% of control for males/females at 3000 ppm], and decreased food efficiency for both sexes at 2000 and 3000 ppm. The 5000 ppm dose group was terminated early [week 8]. The sex organs, pituitary, and adrenals of both sexes appear to be target organs for Iprodione. In general, the decreases observed in organ weights and the accompanying increases in relative organ weights may be attributed to the decreased body weight, but in females, decreased relative organ weights were observed in the uterus, ovary, adrenal, and pituitary, mainly at the high [3000 ppm] dose. These latter decreases and the decrease in absolute brain weight in females appear to be treatment-related. Dose-related microscopic lesions were observed in the sex organs and adrenals of both sexes at the 2000, 3000, and 5000 ppm dose levels. **The NOEL is 1000 ppm [♂♂ 78/♀♀ 89 mg/kg/day], and the LOEL is 2000 ppm [♂♂ 151/♀♀ 184 mg/kg/day], based on decreased body weight/gain, decreased food consumption/ food utilization, organ weight effects, and microscopic lesions in the sex organs.** This study is classified **Acceptable**, although clinical chemistry and hematology parameters were not monitored. This study was performed to determine appropriate dose levels for the 2-year chronic toxicity/ carcinogenicity study in rats, and these parameters were monitored in the long-term study. Therefore, an additional subchronic feeding study in rats is not required [Guideline §82-1(a); MRID 42960701].

In a subchronic feeding study, 2 Beagle dogs/sex/group were administered Iprodione [technical] via the diet at dose levels of 0, 800 ppm [≈60 mg/kg/day], 2400 ppm [≈ 180 mg/kg/day], and 7200 ppm [≈ 270 mg/kg/day] for 90 days [standard conversion of 0.075 used]. There were no deaths. One high-dose dog displayed general fatigue with muscular atony from week 5 to 13. Body weights were comparable among the groups in both sexes. High-dose dogs displayed a slight anemia during the study, and increased alkaline phosphatase and transaminase

[SGOT, SGPT] values compared to the controls. There were no effects reported in clinical chemistry and urinalysis. At necropsy, both females and one male at the high dose displayed slight liver hypertrophy and the other male displayed a pale liver, in addition to anemia and hypertrophy of the prostate and testes. No treatment-related microscopic lesions were observed. **The NOEL is 2400 ppm [≈180 mg/kg/day], and the LOEL is 7200 ppm [≈270 mg/kg/day], based on liver hypertrophy and increased alkaline phosphatase.** This subchronic feeding study in dogs is classified Unacceptable, but there is an acceptable chronic toxicity study in dogs; therefore, an additional subchronic study is not required [Guideline §82-1(b); MRID 00157377, m MRID 00157378, MRID 00232702].

d. Chronic Toxicity and Carcinogenicity

Sufficient data are available to assess the chronic toxicity and carcinogenic potential of Iprodione. Iprodione has been classified as a Group B2 carcinogen, based on evidence of tumors in both sexes of mouse [liver] and in the male rat [Leydig cell]. For the purpose of risk characterization, a low dose extrapolation model was applied to the animal data for quantification of human risk [Q^*_1 = ♂♂ 8.7 x 10^{-3}/♀♀ 5.07 x 10^{-3} combined hepatocellular adenoma/ carcinoma (mouse) and ♂♂ 4.39 x 10^{-2} testicular tumors (rat)].

1.Combined Chronic Toxicity/Carcinogenicity Study in Rats

In the combined chronic toxicity/carcinogenicity study in rats, Iprodione [≈95% a.i.] was administered to 60 Sprague-Dawley rats/ sex/dose via the diet at dose levels of 0, 150, 300, and 1600 ppm [♂♂ 6.1, 12.4, and 69/♀♀ 8.4, 16.5, 95 mg/kg/day, respectively] for 24 months. An additional 10 rats/sex/group were administered Iprodione for 52 weeks [interim sacrifice].

There were no adverse effects on survival or clinical signs in either sex. Body-weight gains were decreased in both sexes at the high-dose level compared to the controls and overall, body-weight gains were 86% and 92% of control values in the high-dose males and females, respectively. At week 12, body-weight gain was 83.6% of the control in males and 80.7% of the control in females at the high-dose level. Food consumption was decreased slightly at this dose level in both sexes also. There were no treatment-related clinical pathology findings in either sex. At the interim sacrifice, high-dose males displayed an increase in the incidence of lesions in the adrenals, and there was an increased incidence of centrilobular hepatocyte enlargement in mid- and high-dose males. High-dose females displayed an increase in centrilobular hepatocyte enlargement and an increase in the incidence of generalized rarefaction and fine vacuolation of the zone fasciculata in the adrenals compared to the control and other dose groups. At the terminal sacrifice, increased liver weight [absolute and relative-to-body] was observed in males at the mid- and high-dose levels [dose-related]. At the high-dose level in males, testes with epididymides and thyroid weights [absolute and relative-to-body] were increased at the terminal sacrifice. At the terminal sacrifice, interstitial cell hyperplasia in the testes, reduced spermatozoa in the epididymides, and absent/empty secretory colloid cells or reduced secretion in the seminal vesicles were observed in the mid- and high-dose males. Atrophy of the seminiferous tubules in the testes, with atrophy of the prostate and absence of spermatozoa in the epididymides were observed at the high-dose level. Centrilobular hepatocyte enlargement was increased in males at the high-dose level. Adrenal lesions were observed in both sexes at the mid- and high-dose levels, although the males displayed more lesions than the females. There was an increased incidence of tubular hyperplasia in the ovaries and increased sciatic nerve fiber degeneration in the high-dose females

compared to the controls. Hemosiderosis was increased in females at the mid- and high-dose levels. **The NOEL for non-neoplastic changes is 150 ppm [♂♂ 6.1/♀♀ 8.4 mg/kg/day], and the LOEL is 300 ppm [♂♂ 12.4/♀♀ 16.5 mg/kg/day], based on increases in generalized enlargement of the cells of the zona glomerulosa in males and females, in fine vacuolation of the zona fasciculata and in generalized fine vacuolation of the zone reticularis in males in the adrenal cortex, an increased incidence of interstitial cell hyperplasia, reduced spermatozoa in the epididymides, reduced secretion of the seminal vesicles, increased hemosiderosis in the spleen in females, and increased liver weight.**

There was an increase in the incidence of both unilateral and bilateral benign interstitial cell tumors in the testes of males at the 1600 ppm dose level. There was a dose-related increasing trend and a significant difference in the pairwise comparison of the 1600 ppm dose group with controls for testicular tumors, which exceeds the historical control incidence [Guideline §83-5; MRID 42637801; MRID 42787001].

In an earlier chronic toxicity/carcinogenicity study in Charles River CD outbred albino rats, no treatment-related tumors were reported, although the incidence of testicular interstitial cell tumors was 2, 2, 4, and 5 out of 60 rats/group at dose levels of 0, 125 ppm [≈6.25 mg/kg/day], 250 ppm [≈12.5 mg/kg/day], and 1000 ppm [≈50 mg/kg/day], respectively [using standard conversion factor of 0.05]. This study is classified Unacceptable, but it was replaced by the study cited above [Guideline §83-5; MRID 00071997; MRID 00128931; MRID 001164249].

2. Chronic Toxicity Study in Dogs

In a chronic feeding study, 6 Beagle dogs/sex/group were administered Iprodione [86.5%] via the diet at dose levels of 0, 100 ppm [♂♂ 4.1/♀♀ 4.3 mg/kg/day], 600 ppm [♂♂ 24.9/♀♀ 28.3 mg/kg/day], and 3600 ppm [♂♂ 145.3/♀♀ 152.5 mg/kg/day] for 12 months. There were no treatment-related deaths, and no adverse effects were observed on body weight, food consumption, or clinical signs in either sex. At the high-dose level, there were increases in absolute and relative liver weight, alkaline phosphatase, SGOT, SGPT and LDH enzyme levels, and increased absolute and relative adrenal weights [both sexes]. At the mid- and high-dose levels, males displayed an increased number of erythrocytes with Heinz bodies and decreased prostate weights. **The NOEL is 100 ppm [♂♂ 4.1/♀♀ 4.3 mg/kg/day], and the LOEL is 600 ppm [♂♂ 24.9/♀♀ 28.3 mg/kg/day], based on decreased prostate weight and an increased incidence of erythrocytes with Heinz bodies** [Guideline §83-1(b); MRID 00144391; MRID 41327001].

In a second chronic feeding study designed to complement the study cited above, 6 Beagle dogs/sex/group were administered Iprodione [96.1%] via the diet at dose levels of 0, 200 ppm [♂♂ 7.8/♀♀ 9.1 mg/kg/day], 300 ppm [♂♂ 12.4/♀♀ 13.1 mg/kg/day], 400 ppm [♂♂ 17.5/♀♀ 18.4], and 600 ppm [♂♂ 24.6/♀♀ 26.4 mg/kg/day] for 12 months. There were no treatment-related deaths, and no adverse effects were observed on clinical signs, body weight/gain, and food consumption in either sex. At the high-dose level, decreases were observed in the red blood cell parameters [hemoglobin, hematocrit, and red blood cells]. **The NOEL for systemic toxicity is 400 ppm [♂♂ 17.5/♀♀ 18.4 mg/kg/day], and the LOEL is 600 ppm [♂♂ 24.6/♀♀ 26.4 mg/kg/day], based on decreased red blood cell values.** This nonguideline study is classified Acceptable. When both chronic dog studies are considered together, the **NOEL is 400 ppm [≈18 mg/kg/day]** [Guideline §83-1(b); MRID 42211101].

3. Carcinogenicity Study in Mice

In a carcinogenicity study, Iprodione [95.7% a.i.] was administered in the diet to 50 Crl: CD-1 (ICR) BR mice/ sex/dose for 99 weeks at dose levels of 0, 160 ppm [♂♂ 23/♀♀ 27 mg/kg/day], 800 ppm [♂♂ 115/♀♀ 138 mg/kg/day], and 4000 ppm [♂♂ 604/♀♀ 793 mg/kg/day]. There was an interim sacrifice group of 15 mice/sex/group.

The statistical evaluation of mortality indicated no significant incremental changes with increasing dose in either sex, although the high-dose group displayed the highest mortality rate for both sexes. Food consumption and clinical signs were comparable among the groups for both sexes. Decreased body- weight gains [overall gain ♂♂ 86%/♀♀ 89% of control] were observed in both sexes at the highest dose level. There was an increase in the incidence of liver tumors in both sexes at the high-dose level, which was accompanied by increases in several liver lesions [centrilobular hepatocyte enlargement/ vacuolation, area(s) of enlarged eosinophilic hepatocytes, pigmented macrophages, centrilobular necrosis, and amyloid deposits]. SGOT and SGPT levels were elevated at the high-dose level in both sexes compared to the controls at the interim sacrifice [only time examined for these enzymes]. Liver weight was increased at the high-dose level in both sexes at both the interim and terminal sacrifices. There was an increase in the incidence of benign ovarian tumors [luteoma] in females at the high dose compared to the control incidence, which was accompanied by an increase in luteinization of the interstitial cells, corpora lutea absent, and prominent granulosa cells. There was also an increased incidence of generalized vacuolation/hypertrophy of the interstitial cells of the testes in the mid- and high-dose males compared to the controls. Dosing was considered adequate, based on an overall decrease in body-weight gain [♂♂ 86%/♀♀ 89% of control]. **The LOEL is 800 ppm [♂♂ 115/♀♀ 138 mg/kg/day], based on the increased incidence of centrilobular hepatocyte enlargement in females and the increased incidence of generalized vacuolation/hypertrophy of the interstitial cells in the testes of males. The NOEL is 160 ppm [♂♂ 23/♀♀ 27 mg/kg/day]** [Guideline §83-2; MRID 42825002].

In a previous chronic toxicity/carcinogenicity study in Carworth CF-1 albino mice, Iprodione was negative for carcinogenicity. The dose levels were 200 ppm [≈30 mg/kg/day], 500 ppm [≈75 mg/kg/day], and 1250 ppm [≈187.5 mg/kg/day] (using standard conversion factor of 0.15), and the duration was 18 months. Only one ovarian tumor [malignant] was reported [mid dose], and the incidence of liver tumors was as follows:

Table 2. Liver Tumors [# with tumor/# mice examined]

Dose/Tumor Type	Benign	Malignant	Dose/ Tumor Type	Benign	Malignant
MALES			FEMALES		
0	0/60	2/60	0	0/60	0/60
200	2/59	0/59	200	1/58	2/58
500	0/60	4/60	500	0/59	1/59
1250	2/59	5/59	1250		

This study is classified Unacceptable, but in has been replaced by the study cited above [Guideline §83-2; MRID 00070963].

4. Studies on Carcinogenicity Mechanism of Action

Several mechanistic studies on Iprodione are available. These were submitted in support of the premise that both the liver and testicular tumors are threshold phenomena.

TESTES

In an in vitro study using immature porcine cultured Leydig cells, Iprodione [99.7%] and two of its metabolites [RP36112 (99.2%) and RP36115 (96.7%)] inhibited testosterone secretion when Leydig cells were stimulated with (1) the gonadotropin hCG, (2) with drugs that enhance cAMP production [(a) cholera toxin, which stimulates Gs protein; (b) forskolin, which stimulates adenylate cyclase catalytic unit, and (3) with a cAMP analog [8-bromo-cAMP]. Because there were no effects observed on gonadotropin-stimulated cAMP production with Iprodione, it is hypothesized that the inhibition of testosterone secretion by Iprodione is downstream from cAMP production. At the next step in testosterone biosynthesis, inhibition of testosterone secretion by Iprodione was not observed when the substrate 22ROHCT was added to the culture medium, which indicates that the step that is inhibited is located between the cAMP production and the movement/penetration of cholesterol into the mitochondria. Since 22ROHCT is a cholesterol substrate that passes through the mitochondrial membrane without the need of an active transport system, the sensitive site of inhibition of testosterone synthesis by Iprodione [or RP 36115] maybe the transport/availability of cholesterol substrate for the cholesterol side chain cleavage enzyme. The RP 36112 metabolite appears to act downstream from the cholesterol step; i.e., at the level of steroidogenic enzyme 17 αhydroxylase/17, 20 lyase. Iprodione and its metabolites appear to modulate Leydig cell steroidogenesis by interfering at the level of cholesterol transport and/or steroidogenic enzyme activity. [Non-Guideline; MRID 44171901].

In another in vitro study, the objective was to determine the effect of in vitro Iprodione [99.7%] exposure on basal testosterone secretion and stimulated release from testicular sections in culture media [in vitro Endocrine Challenge Test (ECT) using human chorionic gonadotropin (hCG)]. The effects of prior in vivo exposure of the male rats via the diet [3000 ppm Iprodione for 14 days] was also evaluated. Testicular sections obtained from 12 male CD® Sprague-Dawley rats administered Iprodione via the diet for 14 days at dose levels of 0 ppm or 3000 ppm were incubated with 0, 1, 10, or 100 µg/mL Iprodione for one hour. Half of these testicular sections from each in vitro treatment group were challenged with human chorionic gonadotrophin and the other half of the sections were monitored for basal testosterone secretion. Media testosterone concentrations were monitored at hourly intervals for 3 hours after challenge. There was a dose-related reduction in testosterone secretion from testicular sections incubated in vitro with Iprodione, with and without hCG stimulation. Prior exposure of the rats to Iprodione in vivo for 14 days appeared to have little effect on the secretion of testosterone, with and without hCG stimulation, from testicular sections incubated in vitro other than a slight increase initially. At sacrifice following the 14-day exposure period to Iprodione in vivo, plasma LH concentrations were significantly increased compared to the control and, although plasma testosterone was not significantly affected, the levels were somewhat increased compared to the control [132% of control]. The significant increase in plasma LH at necropsy suggests a possible stimulation of the homeostatic mechanism. Under the conditions of

this 14-day study. Iprodione was shown to produce a reduction in testosterone secretion from testicular sections following incubation in vitro with Iprodione. Prior exposure of male rats to Iprodione in vivo via the diet for 14 days did not alter the reduction in testosterone secretion observed in their testicular sections exposed to Iprodione in vitro. Although the in vitro inhibition appeared to be dose-related, it appears that a maximum response may have occurred between the 10 and 100 µg/mL dose levels. The data presented provide pieces to the "puzzle" but not a complete picture of what may be occurring in the testes/rat that ultimately results in testicular tumors. Although it appears that the premise is that Iprodione produces testosterone biosynthesis inhibition, resulting ultimately in the increased incidence of Leydig cell tumors, there are inconsistencies in the in vitro and in vivo data, and the in vitro effects observed in the short-term studies to date have not been demonstrated to occur in long-term studies, nor is it clear that the levels at which the in vitro effects were observed are attained in vivo. [Non-Guideline; MRID 44171903].

In an in vivo study, no changes in testicular function, as assessed by measuring testosterone levels in plasma and testicular homogenates from 15 male Sprague-Dawley rats administered Iprodione [97.3%] via the diet at doses levels of 0 ppm and 3000 ppm for 2, 7 or 14 days, were observed. Decreased body weight [95% of control after 2 days, 90-91% of control after 7 days, and 87% of control after 14 days], body-weight gain [negative gain after 2 days, 32% of control after 7 days, 44% of control after 14 days], and food consumption were observed following all exposure intervals. Organ-weight effects included decreased absolute liver, kidney, epididymis, and total accessory sex organs [TASO]; increased absolute and relative adrenal; and decreased relative TASO. The objective of this study was to assess the effects of in vivo Iprodione exposure on plasma and testicular homogenate testosterone concentrations in the male rat following a human chorionic gonadotrophin [hCG] Endocrine Challenge Test (ECT). There were no significant differences in either peripheral plasma or testicular homogenate testosterone levels observed in samples collected one hour after human chorionic gonadotrophin [hCG] challenge. Under the conditions of this study, Iprodione did not produce alterations in testicular function following dietary exposure at 3000 ppm for up to 14 days [Non-Guideline; MRID 44171904].

In a mechanistic study in male rats designed to (a) assess the competitive binding affinity of Iprodione to the androgen receptor; (b) establish an effective dose and dosing regimen and quantify testosterone, luteinizing hormone [LH], follicle-stimulating hormone [FSH], and estradiol concentrations in a single plasma sample; and © describe testosterone, LH, and FSH profiles during a 4-hour baseline occurring after 30 days of Iprodione exposure, Iprodione was shown to have poor binding affinity to the androgen receptor following exposure at very high dose levels. LH and FSH concentrations were increased after 15 days exposure but not after 30 days of exposure to Iprodione. At necropsy, testosterone concentrations were comparable between the Iprodione and the pair-fed rats, and estradiol concentrations were increased at necropsy following 30 days of exposure. A marked increase in adrenal weights was accompanied by histopathological lesions [vacuolation] indicative of an alteration of steroidogenesis was observed following the 30-day exposure period. Although there was some evidence to suggest that Iprodione interferes with sex/steroid hormone regulation, the difference in the spectrum of effects observed between Iprodione and Flutamide in this study indicate that the two compounds share only certain parts of a mechanism of toxicity/carcinogenicity. [Non-Guideline; MRID 43535002; MRID 44203401].

In an in vitro study using porcine cultured Leydig cells, Iprodione [99.7%] and two of its metabolites were shown to inhibit gonadotropin-stimulated testosterone secretion in a concentration range of 1-10 µg/mL. Inhibition by Iprodione was observed after short-term exposure [3 hours], and the inhibitory effects were similar

to those observed with the fungicide Ketoconazole. The inhibitory effects do not appear to be related to Leydig cell damage because the removal of Iprodione from the culture medium for 72 hours resulted in the recovery of the cells ability to secrete testosterone following hCG stimulation. There was no discussion as to how the concentrations of Iprodione used in this study relate to the levels attained within the testicular cells following oral dosing in the rat carcinogenic study where testicular tumors were observed. [Non-Guideline; MRID 43830601].

LIVER

In a 3-day and 14-day oral exposure study, groups of CD1 male mice [15/dose/group/chemical; 7 weeks old on arrival] were administered (1) **IPRODIONE** via the diet at dose levels of 4000 ppm [696 mg/kg/day] or 12000 ppm [2138 mg/kg/day]; (2) **KETOCONAZOLE** via the diet at a dose of 2000 ppm [341 mg/kg/day]; (3) **PHENOBARBITAL** via gavage at a dose level of 75 mg/kg/day; and (4) **CYPROTERONE ACETATE** via gavage at a dose level of 40 mg/kg/day. The control for the dietary studies was basal diet, and 0.5% methylcellulose was the control of the gavage studies. The objective of the study was to examine the potential liver effects of Iprodione in mice and to compare these effects with those produced by well characterized liver enzyme inducers and/or rodent liver carcinogens. Ketoconazole was selected as a positive control for its potential to inhibit testosterone secretion; Phenobarbital and Cyproterone acetate were selected for their potential to induce early liver changes and subsequent liver tumor formation in rodents. All of the liver effects produced by Ketoconazole, Phenobarbital, and/or Cyproterone acetate [increases in liver weight, alanine aminotransferase, aspartate aminotransferase, # hepatocytic mitoses, total cytochrome P-450 content, staining for isoforms CYP 2B and CYP 3A, benzoxyresorufin [BROD], ethoxyresorufin [EROD], pentoxyresorufin [PROD] enzyme activities, and hepatocyte proliferation, in addition to increases in the incidence of liver enlargement, centrilobular hypertrophy, diffuse hypertrophy, centrilobular/midzonal fine vacuolation] were exhibited by Iprodione at 12000 ppm. An effect observed following Iprodione exposure that was not observed following any of the other test material exposures was an increase in lauric acid hydroxylation. Although several of the effects observed in the liver following Iprodione exposure are analogous to those observed following the positive controls, especially Phenobarbital [centrilobular hypertrophy, liver weight, increased BROD, PROD, and EROD activities, cell proliferation after 3 days], in several cases the liver effect observed was most pronounced in the Iprodione mice compared to the positive controls [centrilobular/midzonal fine vacuolation, increased number of mitoses, cell proliferation at day 15].
This study demonstrates that Iprodione, at dose levels that are 5- and 15- fold greater than the LOEL for liver effects observed in the mouse carcinogenicity study, induces (1) liver cell proliferation, (2) increased microsomal enzyme activities, (3) an increase in total cytochrome P-450 content, and (4) centrilobular hypertrophy. These observations most closely resemble the pattern of liver effects observed following Phenobarbital exposure. Hepatocytic hypertrophy was observed at the high-dose level of Iprodione following both the 3- and 14-day exposure periods but only following the 14-day exposure period at the low dose. Liver cell proliferation was observed after both the 3-day and 14-day exposure periods at both dose levels of Iprodione. Increased cytochrome P-450 content and increased microsomal enzyme activities were observed at both dose levels of Iprodione following the 14-day exposure period, but neither analysis was performed following the 3-day exposure period. The dose level where liver tumors were observed in the mouse carcinogenicity study [604 mg/kg/day] is comparable to the low dose used in the current study. The findings in this study support the Registrant's arguments that the liver tumors observed in the Iprodione mouse

carcinogenicity study may be secondary to liver toxicity. However, several pieces of data are lacking. The current study does not address whether cytochrome P-450 content and the microsomal enzyme activities are increased initially [after the 3-day exposure period]; therefore, one cannot determine whether the cell proliferation and hepatocytic hypertrophy observed after 3-days exposure to Iprodione is due to a direct effect of Iprodione on the liver or the result of adaptive processes. Additionally, the current study does not identify a NOEL for the liver effects monitored over a 14-day exposure period or address the question of whether these liver effects occur initially at the lower doses utilized in the mouse carcinogenicity study. Another outstanding question is whether the liver effects [hepatocytic hypertrophy, increased total cytochrome P-450 content, increased microsomal activities, cell proliferation] observed in the current study persist throughout a long-term exposure. It is to be noted that Phenobarbital produces a short-term increase in hepatocyte proliferation that is not sustained [Jirtle, et al. 1991, Standeven and Goldsworthy, 1993]. In a paper on proliferation and liver tumor development [CIIT Activities, vol. 15 (8), August, 1995], it is stated that the proliferative response seen after acute exposure does not always reflect the proliferative response observed after chronic exposure [Non-Guideline; MRID # 44171902]].

Based on these mechanistic studies, HED's Cancer Assessment Review Committee (CARC) concluded that the data available do not provide a definitive mode of action with respect to either the Leydig cell tumors or the liver tumors (reference 1997).

e. Reproduction and Developmental Toxicity Studies

1. Two-Generation Reproduction Study in Rats

In a 2-generation reproduction study, 28 Crl:CD®BR/VAF/PLUS rats/sex/group were administered Iprodione [96.2%] via the diet at dose levels of 0, 300 ppm [♂♂ 18.5/♀♀ 22.5 mg/kg/day], 1000 ppm [♂♂ 61.4/♀♀ 76.2 mg/kg/day], and 3000/2000 ppm [♂♂ 154.8/♀♀ 201.2 mg/kg/day] for two generations [2 litters per generation]. **The systemic maternal/parental NOEL was 300 ppm [♂♂ 18.5/♀♀ 22.5 mg/kg/day], and the LOEL was 1000 ppm [♂♂ 61.4/♀♀ 76.2 mg/kg/day], based on decreased body weight, body-weight gain, and food consumption in both sexes and both generations. The reproductive [offspring] NOEL was 1000 ppm [76.2 mg/kg/day], and the reproductive [offspring] LOEL was 2000 ppm [201.2 mg/kg/day], based on decreased pup viability [as evidenced by an increased number of stillborn pups and decreased survival during postnatal days 0-4], decreased pup body weight throughout lactation, and an increased incidence in clinical signs in pups during the lactation period [smallness, reduced mobility, unkempt appearance, hunching, and/or tremors]** [Guideline §83-4; MRID 00162983; MRID 41871601].

2. Developmental Toxicity Study in Rats

In a developmental toxicity study, 20 pregnant Sprague-Dawley CD rats [mated 1:1] were administered Iprodione [94.2%] at dose levels of 0 [0.5% methylcellulose], 40, 90, and 200 mg/kg/day via gavage from day 6 through 15 of gestation. On day 20 of gestation, the dams were sacrificed via CO_2 inhalation. There were no deaths. Body weights were comparable among the groups. There were no significant differences observed in the mean number of viable fetuses, implantations, corpora lutea, resorptions, and pre- and postimplantation losses were comparable among the groups. There was no evidence of maternal toxicity at any dose level. **The**

developmental NOEL was 90 mg/kg/day, and the developmental toxicity LOEL was 200 mg/kg/day, based on delayed fetal development [slightly reduced fetal body weight and increased incidences of space between the body wall and organs in the fetuses]. [Guideline §83-3(a); MRID 00162984; MRID 40514901].

In a 1976 prenatal developmental toxicity study, groups of pregnant Sprague-Dawley rats (25-30/dose) received Iprodione (100%) in 1% carboxymethylcellulose via gavage at doses of 0, 100, 200, or 400 mg/kg/day during gestation days 5 through 15. For maternal toxicity, the NOEL was 200 mg/kg/day and the LOEL was 400 mg/kg/day based on slightly decreased body weight gain and significantly decreased food consumption. For developmental toxicity, the NOEL was 200 mg/kg/day and the LOEL was 400 mg/kg/day based on decreased implantation sites. This study does not appear to provide a robust evaluation of fetal effects following *in utero* exposure of Iprodione (MRID 0071324).

In a 1997 special prenatal developmental toxicity study, pregnant Sprague-Dawley rats (25/dose) received Iprodione (97.1%)in methylcellulose via gavage at dose levels of 0, 20, 120, or 250 mg/kg/day during gestation days 6 through 19. For maternal toxicity, the NOEL was 20 mg/kg/day, the LOEL was 120 mg/kg/day, based on decreased body-weight gain and decreased food efficiency. At 250 mg/kg/day, deaths occurred [9 out of 25] in addition to decreased body-weight gain and food consumption/ efficiency. For developmental toxicity, the NOEL was 20 mg/kg/day and the LOEL was 120 mg/kg/day, based on decreased anogenital distance (AGD) in the male pups (MRID No. 44365001).

3. Developmental Toxicity Study in Rabbits

In a developmental toxicity study, 18 artificially inseminated New Zealand female rabbits were administered Iprodione [95.0-99.3%] at dose levels of 0 [0.5% aqueous methylcellulose], 20, 60, and 200 mg/kg/day via gavage from day 6 through 18 of gestation. On day 29 of gestation, the does were sacrificed. Seven high-dose does aborted between days 17 and 23 of gestation, and prior to aborting all had displayed decreased urination and defecation. One mid-dose doe [day 28] and one control doe [day 20] also aborted. All other does survived until study termination, and nine of the high-dose does that did not abort displayed decreased urination and defecation. During the dosing period, the mid-dose does gained less weight than the control, and the high-dose does lost weight. A negative net body-weight gain was observed at the mid- and high-dose levels. The high-dose does displayed decreased food consumption during the dosing period. Gravid uterine weight was decreased at the high-dose level [90% of control] compared to the control. **The maternal NOEL is 20 mg/kg/day, and the maternal LOEL is 60 mg/kg/day, based on decreased body-weight gain. At the highest dose tested [200 mg/kg/day], maternal toxicity was demonstrated by an increased rate of abortions [7 does], body-weight loss, decreased food consumption, and decreased defecation and urination in females that aborted. The developmental toxicity NOEL was 60 mg/kg/day, and the developmental toxicity LOEL was 200 mg/kg/day, based on an increased incidence of skeletal variations [13th full rib, malaligned sternebrae, and/or 27 presacral vertebrae, with or without delayed ossification].** [Guideline §83-3(b); MRID 00155469].

Due to the structural similarity of Iprodione to Procymidone and Vinclozolin and to the observed effects on the reproductive system in males in the long-term feeding study in rats, a pre-and postnatal developmental toxicity study is required to assess the effects of Iprodione on the male reproductive system. for Iprodione. These effects

can e addressed by adhering to the new guidelines for reproductive toxicity. OPPTS 870.3800. This study is required.

f. Mutagenicity Studies

Sufficient data are available to satisfy data requirements for mutagenicity testing [§84-2].

1. Gene Mutation

Iprodione was **negative** for induction of reverse gene mutations at the histidine locus in Salmonella typhimurium strains TA 98, TA 100, TA1535, TA 1537, and TA 1538, both in the presence and absence of S9 activation. There was sufficient cytotoxicity, as evidenced by reductions in mean numbers of revertants and background lawn, at the highest dose in the absence of S9, and a slight to moderate precipitate was observed at doses ≥ 250 µg/plate in the presence and absence of S9. In the presence of S9, Iprodione was assayed to the limit dose [Guideline §84-2; MRID 41604106].

Iprodione **did not induce mutation with or without metabolic activation** in the in vitro forward gene mutation [CHO/HGPRT] assay at adequate dose levels [Guideline §84-2; MRID 00148206].

2. Chromosomal Aberration Assay

Iprodione was **negative** in an in vitro chromosomal aberration assay in Chinese hamster ovary [CHO] cells both in the presence and absence of metabolic activation at adequately high dose levels [doses of 40, 150, 400 µg/mL with; doses of 15, 75, 150 µg/mL without S9]. There was precipitation at exposure levels ≥150 µg/mL both with and without S9. [Guideline §84-2; MRID 00148207].

In an in vivo mouse micronucleus assay, 5 CD-1 mice/sex/group were administered Iprodione [96.1%] suspensions [1% aqueous methylcellulose] via oral gavage once at dose levels of 750, 1500, and 3000 mg/kg. Bone marrow cells were collected for micronucleated polychromatic erythrocytes [MPEs]. One male and eight females died at the high dose, and signs of toxicity at this dose level included piloerection, hunched posture, ptosis, lethargy, and coma. Dose-related cytotoxic effects on the target tissue were also seen at 48 hours postdose; the response was significant at the high dose. The positive control induced the expected high yield of MPEs in both sexes. **There was no evidence of a clastogenic or aneugenic effect at any dose or harvest time** [Guideline §84-2; MRID 43535001].

3. Other Genotoxic Effects

Iprodione was **negative in a sister chromatid exchange assay in Chinese hamster ovary cells both with and without metabolic activation** [Guideline §84-2; MRID 00148209].

Iprodione was tested against 19 strains [including 2 wild type] of Bacillus subtilis both with and without metabolic activation at dose levels of 20.6-1670 µg/disc. Iprodione was **positive both with and without metabolic activation** [Guideline §84-2; MRID 00148208].

g. Metabolism

Sufficient data are available on the metabolism of Iprodione in the rat.

^{14}C-Iprodione was absorbed readily from the gastrointestinal tract, metabolized, and excreted by rats of both sexes following single low [50 mg/kg] and high [900 mg/kg] oral doses and 14 repeated low [50 mg/kg/day] doses. Peak blood levels were observed at 4 and 2 hours, respectively, in the low-dose males and females and at 6 hours in the high-dose rats of both sexes. The elimination of ^{14}C from the blood was slower in males than in females. There were both dose- and sex-related differences noted in absorption; males absorbed a greater percentage of the low and repeated doses than females. Although levels of ^{14}C were found in most tissues monitored, the levels were ≤ 0.5% of the total amount administered. It is to be noted that the testes of the low-dose males [both single and repeat] showed no detectable amount of ^{14}C; the high dose in the rat chronic toxicity/ carcinogenicity study where testicular tumors were observed was 69 mg/kg/day. The primary route of elimination of ^{14}C following single and repeat low dose exposure was the urine, and the feces was the primary route following high-dose exposure. Dealkylation and cleavage of the hydantoin ring were the two primary steps in the metabolism of Iprodione. Hydroxylation of the phenyl ring and oxidation of the alkyl chain also occurred. The primary metabolites recovered from the urine [both sexes] included a dealyklated derivative of Iprodione and 2 polar but unidentified compounds. Males produced larger amounts of a hydantoin ring-opened metabolite than females, and the urine of the females contained a higher proportion of unchanged parent than that of the males. Several urinary metabolites were not identified. The feces contained much larger amounts of unchanged parent than the urine, which the authors suggested was unabsorbed Iprodione and metabolites or hydrolyzed conjugates of absorbed material.

In another single oral administration study in rats using 50 mg/kg, no sex differences were apparent in the excretion profile, and both urinary elimination [♂♂ 37%/♀♀ 28%] and fecal excretion [♂♂ 56%/♀♀ 50%] were major routes of excretion, and the majority of the radiolabel was excreted within the first 24 hours post dose in both sexes. Approximately 80% of the 24-hour urine sample radiolabel [≈24% of the dose] and ≈91% of the 24-hour fecal radiolabel [≈49% of the dose] were characterized. Overall, ≈72% of the dose was identified, which accounted for nearly 90% of the total radiolabel found in the samples. The metabolism of Iprodione was extensive and characterized by the large number of metabolites formed. In the urine, RP 36115, RP 32490, RP 36112, RP 36119, and RP 30228 were either confirmed or indicated. The feces contained a large proportion of parent; the major fecal metabolites were RP 36115, RP 36114, RP 32490, and RP 30228.

A general metabolic pathway for Iprodione in the rat indicates that biotransformation results in hydroxylation of the aromatic ring, degradation of the isopropylcarbamoyl chain, and rearrangement followed by cleavage of the hydantoin moiety. Additionally, structural isomers of Iprodione resulting from molecular rearrangement, as well as intermediates in the pathway, were detected [Guideline §85-1; MRID 41346701; MRID 42984101; MRID 43484901].

h. Dermal Penetration Study

In a dermal penetration study, 4 male Crl: CD®BR rats/group/time point were exposed dermally to a single dose of Iprodione at dose levels of 0.4, 4.0, and 40 mg/rat for 0.5, 1, 2, 4, 10, and 24 hours. Skin residues increased

with the duration of exposure to 5-10% of the applied dose, although there was no apparent dose response. The portion of the test material absorbed increased with the duration of exposure to 7.41%, 3.16%, and 0.19% of the applied dose at 0.4, 4.0, and 40 mg/rat, respectively. Absorption appears to be saturated at the two highest dose levels. Following a 10-hour exposure period, ≈5% Iprodione is absorbed [Guideline §85-2; MRID 43535003].

I. Inhalation Toxicity

The only inhalation study available for Iprodione is an acute inhalation toxicity study, with an acute $_{LC50}$ = 5.16 mg/L [MRID 42946101]. These results place Iprodione in Toxicity Category IV. No other studies are available via this route.

2. Dose/Response Assessment

The dose-response assessment for Iprodione was conducted by OPP's toxicology peer review committees, who selected risk assessment endpoints after reviewing the entire toxicology database for Iprodione. A brief history of the findings of OPP's peer review committees is presented below.

On February 10, 1994 the Health Effects Division's RfD/Peer Review Committee established a Reference Dose (RfD) of 0.06 mg/kg/day based on a NOEL of 6.1 mg/kg/day established in a combined chronic toxicity/carcinogenicity study in rats and an Uncertainty Factor of 100 for inter-species extrapolation and intra-species variability (Ghali 1994).

On May 1, 1997, the Health Effects Division's Toxicology Endpoint Selection (TES) Committee selected the doses and endpoints for acute dietary as well as occupational and residential exposure risk assessments (USEPA 1997).

On October 16, 1997, the Health Effects Division's Hazard Identification Assessment Review Committee (HIARC) evaluated the toxicology data to assess the potential enhanced sensitivity of infants and children from exposure to Iprodione as required by the Food Quality Protection Act (FQPA) of 1996 (Ghali 1997).
On February 25, 1998, the HIARC met again to re-evaluate the toxicological endpoints for acute and chronic dietary as well as occupational and residential (dermal and inhalation) exposure risk assessments in light of a recently submitted special prenatal developmental toxicity sexual differentiation study in rats (MRID No. 44365001). The HIARC determined that the application of the FQPA safety factor for the protection of infants and children from exposure to Iprodione, as required by FQPA, would be determined during risk characterization, by the new OPP FQPA Safety Factor Committee (Rowland and Taylor 1998) .

a. FQPA Considerations

1. Neurotoxicity Data

There are no acute and subchronic neurotoxicity studies for Iprodione.

2. Developmental Toxicity Data

In a 1976 prenatal developmental toxicity study, groups of pregnant Sprague-Dawley rats (25-30/dose) received Iprodione (100%) in 1% carboxymethylcellulose via gavage at doses of 0, 100, 200, or 400 mg/kg/day during gestation days 5 through 15. For maternal toxicity, the NOEL was 200 mg/kg/day and the LOEL was 400 mg/kg/day based on slightly decreased body weight gain and significantly decreased food consumption. For developmental toxicity, the NOEL was 200 mg/kg/day and the LOEL was 400 mg/kg/day based on decreased implantation sites. This study does not appear to provide a robust evaluation of fetal effects following *in utero* exposure of Iprodione (MRID 0071324).

In a 1986 prenatal developmental toxicity study, groups of pregnant Sprague-Dawley rats were given oral (gavage) administrations of Iprodione (94.2%) in 0.5% methylcellulose at doses of 0, 40, 90, or 200 mg/kg/day during gestation days 6 through 15. No maternal toxicity was observed (maternal NOEL $\geq$200 mg/kg/day). For developmental toxicity, the NOEL was 90 mg/kg/day and the LOEL was 200 mg/kg/day, based upon delayed fetal development, as evidenced by slightly reduced fetal weights and an increased incidence of space between the body wall and organs in fetuses(MRID 00162984).

In a 1997 special prenatal developmental toxicity study, pregnant Sprague-Dawley rats (25/dose) received Iprodione (97.1%) in methylcellulose via gavage at dose levels of 0, 20, 120, or 250 mg/kg/day during gestation days 6 through 19. For maternal toxicity, the NOEL was 20 mg/kg/day, the LOEL was 120 mg/kg/day, based on decreased body-weight gain and decreased food efficiency. At 250 mg/kg/day, deaths occurred [9 out of 25] in addition to decreased body-weight gain and food consumption/ efficiency. For developmental toxicity, the NOEL was 20 mg/kg/day and the LOEL was 120 mg/kg/day, based on decreased anogenital distance in the male pups (MRID No. 44365001).

In a prenatal developmental toxicity study, pregnant New Zealand white rabbits (18/group), were given oral (gavage) administration of Iprodione (95% or 99.3%, from two different lots) in 0.5% Methocel at doses of 0, 20, 60, or 200 mg/kg/day during gestation days 6 through 18. For maternal toxicity, the NOEL was 20 mg/kg/day and the LOEL was 60 mg/kg/day based on decreased body weight gain. Also at 200 mg/kg/day, the following were observed: increased numbers of abortions, body weight loss, decreased food consumption and decreased defecation and urination. For developmental toxicity, the NOEL was 60 mg/kg/day and the LOEL was 200 mg/kg/day based upon increased skeletal variations (13th full rib, malaligned sternebrae, and 27 presacral vertebrae, occurring alone or in combination with each other or accompanied by delayed ossification) (MRID No. 00155469).

3. Reproductive Toxicity Data

In a two-generation reproduction study, male and female Sprague-Dawley received diets containing Iprodione (96.2%) at 0, 300, 1000, or 2000/3000 ppm (0, 18.5, 61.4, or 154.8 mg/kg/day for males and 22.49, 76.2, or 201.2 mg/kg/day for females) For parental systemic toxicity, the NOEL was 300 ppm (21 mg/kg/day) and the LOEL was 1000 ppm (69 mg/kg/day), based on decreased body weight, body weight gain, and food consumption in both sexes and generations. For offspring toxicity, the NOEL was 1000 ppm (69 mg/kg/day) and the LOEL was 2000/3000 ppm (178 mg/kg/day), based on decreased pup viability (as evidenced by an

increased number of stillborn pups and decreased survival during postnatal days 0-4). decreased pup body weight throughout lactation. and an increased incidence in clinical signs (smallness. reduced mobility. unkempt appearance. hunching, and/or tremors) in pups during the lactation period. (MRID No. 41871601).

4. Determination of Susceptibility

The prenatal developmental toxicity study in rabbits, the special prenatal study in rats, and the two-generation reproduction study in rats demonstrated no indication of increased susceptibility to *in utero* and/or postnatal exposure to Iprodione.

In the 1986 prenatal developmental toxicity study in rats, however, developmental effects in the fetuses (a slight dose-related decrease in fetal weight and increased incidence of fetuses with a space between the body wall and the internal organs) were noted in the absence of maternal toxicity. It is noted that the fetal findings were suggestive but not conclusive of fetal toxicity. Fetal weights were not altered in a statistically significant manner and were well within historical values. The incidence of space between the body wall and organs was also not apparently statistically significant. This finding may have been supportive (as were the c-section observations of "small fetus") of weight decrements in fetuses at the LOEL, but it could also be an artifact of preservative techniques. Also, the fetal findings were marginal and not statistically significant, within ranges of historical control values, and were not supported by data from other studies. Therefore, due to the lack of confidence in these data, the findings of this study were not judged to be an appropriate measure of potential sensitivity following *in utero* exposure to Iprodione.

Based on the weight-of-the-evidence of all available studies, the Committee concluded that there was no increased susceptibility to rat and rabbit fetuses following *in utero* and/or post natal exposure to Iprodione.

5. Recommendation for a Developmental Neurotoxicity Study

Based on the following weight-of-the-evidence considerations, the HIARC determined that a developmental neurotoxicity study in rats is **not** required for Iprodione.

(I) Evidence that support not requiring a developmental neurotoxicity study:

- Overall, Iprodione does not appear to be a frankly neurotoxic chemical. There were no effects on brain weight or histopathology (nonperfused) of the nervous system in the chronic studies in rats, mice, and dogs. Findings that were suggestive of neurotoxicity (see below) were often equivocal, unsupported by data from other studies, and/or observed only at doses which compromised the survival of the animals.

- No evidence of developmental anomalies of the fetal nervous system was observed in the prenatal developmental toxicity studies in either rats or rabbits, at developmentally and/or maternally toxic oral doses up to 200 mg/kg/day.

- Evaluation of the special postnatal developmental toxicity study did not reveal any endpoints of concern that would trigger a developmental neurotoxicity study.

(ii) Evidence that would suggest the need for a developmental neurotoxicity study:

- In the chronic toxicity study in rats, degeneration of the sciatic nerve was observed after 2 years of dietary exposure to Iprodione. This finding was also observed at a relatively high incidence in control animals, although the incidence doubled for females at the highest dose tested (1600 ppm).

- In the carcinogenicity study in mice, absolute brain weight was slightly decreased and adjusted brain weight was significantly decreased at the HDT (4000 ppm).

- In the 90-day subchronic study in rats, absolute brain weight was significantly decreased for females only at the HDT (3000 ppm). Clinical signs of toxicity in this study included piloerection and hunched posture at 3000 and 5000 ppm (the 5000 ppm treatment group was terminated early due to severe toxicity).

- In the two-generation reproduction study in rats, clinical observations in pups included reduced mobility, unkempt appearance, hunching, and/or tremors at the HDT (2000/3000 ppm = 178 mg/kg/day). At this treatment level, severe toxicity was observed in the parental animals, pup body weight was reduced, and pup survival was compromised.

- Iprodione causes endocrine disruption, affecting the reproductive system, pituitary, adrenals, and/or thyroid in various studies.

(iii) Other Unknown Factors:

- Because of the lack of acute and subchronic neurotoxicity studies in rats, there was no evaluation of the nervous system following perfusion. Findings in other studies that were suggestive of neurotoxicity could not be confirmed or refuted.

b. FQPA Uncertainty / Safety Factor

The decision to apply an additional safety factor to ensure the protection of infants and children from exposure to Iprodione, as required by FQPA, was elevated to the OPP Division Directors, who met to discuss the Iprodione FQPA Safety Factor on April 7, 1997. The Division Directors decision and decision logic is summarized below (Tarplee and Rowland 1997).

1. Determination of the Factor. It was determined that **the additional 10x Safety Factor** for enhanced sensitivity to infants and children (as required by FQPA) **should be reduced to 3x.**

2. Rationale for Selection of the FQPA Factor. The rationale for reducing the 10x factor to 3x are as follows:

- No enhanced susceptibility was seen in rat and rabbit developmental and the two generation reproduction study in rats.

- The critical endpoint for acute dietary risk assesssment (decreased AGD) was seen at a high dose (120 mg/kg/day) and there were only marginal differences in the degree of decreased AGD between the doses 20 mg/kg/day (2.44), 120 mg/kg/day (2.32) and 250 mg/kg/day (2.10) thus indicating the "true" NOEL could be higher than the one established at 20 mg/kg/day.

- The proposed mode of action of Iprodione is disruption of testosterone biosynthesis.

- The use of a realistic dietary exposure data (refined using monitoring data and percent crop treated).

- The endpoints selected for both the acute (AGD) and the chronic (histopathology of male reproductive system) risk assessments are based on developmental/reproductive effects.

- The uncertainty with regard to the pre/post natal exposure study requested by the HIARC which may confirm the effects seen in the standard developmental/reproductive studies.

3. Identification of Population Subgroups to receive the Safety Factor

I. Acute Dietary Risk Assessment. The FQPA Safety Factor will be applied for acute dietary risk assessment for **Females 13 + only** because the endpoint (decreased AGD) is an *in utero* effect occurring during prenatal exposure. An appropriate endpoint attributable to a single dose was not identified for the General Population including Infants and Children for this risk assessment. Since the decreased AGD occurs during *in utero* exposure, it is not an appropriate endpoint for acute dietary risk assessment of Infants and Children (i.e., the anogenital distance can not be altered after birth in Infants and Children).

ii. Chronic Dietary Risk Assessment. The FQPA Safety Factor will be applied for chronic dietary risk assessment for the General Population including Infants and Children since the endpoint is based on reproductive effects (histopathological lesions in the male reproductive organs).

iii. Occupational Exposure. The FQPA Safety Factor will not be applied to any occupational scenarios, as per Agency policy.

iv. Residential Exposure. The FQPA Safety Factor will be applied to residential exposure risk assessments for Female 13 + as well as the General Population including Infants and Children due to the potential exposure by these subpopulations based on the use pattern (ornamental lawn and turf) and the inhalation endpoint is based on reproductive effects in a chronic rat study (NOEL of 6.1 mg/kg/day).

c. Toxicological Endpoints for Risk Assessment

1. Acute Dietary

The HAZID Committee of February 25, 1998 determined that the developmental NOEL of 20 mg/kg/day based on decreased anogenital distance (AGD) in male fetuses at 120 mg/kg/day (LOEL should be used to establish the Acute RfD. This NOEL is from a special rat developmental study (MRID 44365001) which was designed to determine the impact of Iprodione on sexual differentiation. This endpoint applies only for females 13+. The acute FQPA RfD for Iprodione was calculated to be 0.06 mg/kg/day for females 13+ and 0.2 mg/kg/day for all other populations using the formula given below:

$$\textbf{Acute RfD} = \frac{\text{20 mg/kg/day (NOEL)}}{100} = 0.02 \text{ mg/kg/day}$$

where the UF of 100X is for inter- and intra-species variability.

For females 13+, the Acute RfD was adjusted with an additional 3X uncertainty factor to account for FQPA considerations. The resulting acute FQPA RfD for acute dietary risk assessment is calculated to be 0.06 mg/kg/day using the formula given below:

$$\text{FQPA acute RfD} = \frac{\text{0.02 mg/kg/day}}{3} = 0.06 \text{ mg/kg/day}$$

As noted previously, an acute dietary toxciological endpoint was not identified for the general population.

The target acute dietary MOE for Iprodione is 300, based on uncertainty factors of 10X for interspecies variability, 10X for intraspecies variability, and 3X for FQPA considerations.

The HIARC selected the dose of 20 mg/kg/day from the special rat study as a conservative estimate for risk assessment, however, doubted if this dose represented a "true" NOEL for the following reasons: 1) effects at the next higher dose (120 mg/kg/day, the LOEL), consisted of only marginal decreases; 2) although the decrease in AGD at the LOEL showed statistical significance, the biological significance is questionable because of the extent of the decreases seen between the NOEL (2.44±0.14) and the LOEL (2.32±0.12) which indicate that the "actual" no effect level could be higher, some where in between these levels (i.e, 20 and 120 mg/kg/day); 3) lack of evaluation of another critical endpoint (i.e., nipple development, characterized as areolas/nipple anlagen in two strains of rats) which was observed along with the decrease in AGD with Vinclozolin, a structurally related compound; and 4) although AGD was not measured, another developmental toxicity study in rats demonstrated a developmental NOEL of 90 mg/kg/day based on delayed fetal development (MRID 00162984).

The HIARC noted that the TES Committee selected the NOEL of 90 mg/kg/day established in the 1986 study along with an additional Uncertainty Factor of 3 due to the lack of data on the androgen deprivation effect. This yielded a dose (90÷3=30 mg/kg/day) which is comparable to the 20 mg/kg/day dose selected for this risk assessment.

2. Chronic Dietary

i. Reference Dose (RfD)

The February 28, 1998 HIARC re-affirmed the dose and endpoints selected for establishing the chronic RfD in 1994 (Rowland 1998). The chronic RfD was based on a NOEL of 6.1 mg/kg/day from a rat combined chronic toxicity/carcinogenicity study (MRID 42637801; MRID 42787001]) based on histopathological lesions in the male reproductive system and effects on the adrenal glands in males at 12.4 and in females at 16.5 mg/kg/day (LOEL). The NOEL was adjusted with an uncertainty factor of 300 (10 x for inter-species extrapolation and 10 x for intra-species variability and 3X for FQPA considerations). The chronic FQPA RfD was determined to be 0.02 mg/kg/day.

$$\textbf{Chronic FQPA RfD} = \frac{\text{6.1 mg/kg/day (NOEL)}}{\text{300 (UF)}} = \textbf{0.02 mg/kg/day}$$

Iprodione has been reviewed by the FAO/WHO Joint Committee Meeting on Pesticide Residues [JMPR]. The World Health Organization (WHO) established an acceptable daily intake (ADI) of 0.3 mg/kg/day in 1977. This ADI was revised to 0.2 mg/kg/day in 1992.

ii. Carcinogenic Risk Assessment

HED's Cancer Assessment Review Committee (CARC) in accordance with the EPA *Proposed Guidelines for Carcinogen Risk Assessment* (April 10, 1996), classified Iprodione as a **"likely"** human carcinogen based on the combined hepatocellular adenomas/ carcinomas in mice and testicular tumors in male rats with a linear low-dose extrapolation approach and a 3/4s interspecies scaling factor for human risk characterization. For the combined hepatocellular adenomas/ carcinomas, the Q_1*s are 8.7×10^{-3} for the male mouse and 5.07×10^{-3} for the female mouse. For the Leydig cell tumors in male rats, the Q_1* is 4.39×10^{-2}. The CARC determined that of these, the most potent Q_1* of 4.39×10^{-2} should be used for cancer risk assessments. Therefore, the Q_1* of 4.39×10^{-2} should be used for estimating carcinogenic risk.

3. Occupational/Residential Exposure

i. Dermal Absorption

The HIARC determined the dermal absorption factor for Iprodione to be 5% at 10 hours. This factor is necessary ONLY for Long-Term chronic and carcinogenic dermal risk assessments since Short-and Intermediate-Term risk assessments are not required. This dermal absorption factor is based on MRID No. 43535003.

ii. Short- and Intermediate-Term Dermal - (1 days to several months)

The HIARC determined that these endpoints are not applicable to Iprodione. No dermal or systemic toxicity was seen following repeated dermal application of Iprodione at 0, 100, 500 or 1000 mg/kg/day, 6 hours/day, 5 days/week over a three week period to male and female New Zealand rabbits (MRID No. 42032301). The HIARC concurred with the TES Committee's conclusions that there is no potential hazard via the dermal route because of the lack of systemic toxicity at the Limit-Dose (1000 mg/kg/day) and the demonstration of low (5%) absorption via the dermal route. This risk assessment is **NOT** required.

iii. Long-Term Dermal (Several Months to Life-Time)

(A). Non-Cancer (Chronic) Effects. A NOEL of 6.1 mg/kg/day from a combined rat chronic toxicity/carcinogenicity study (MRID Nos. 43308201 & 43000501) was chosen for chronic dermal risk assessment. The NOEL of 6.1 mg/kg/day was based on histopathological lesions in the male reproductive system and effects on the adrenal glands in males at 12.4 and in females at 16.5 mg/kg/day (LOEL). This dose was selected since the current use pattern (6 days/week for up to 180 days) indicates potential for Long-Term dermal exposures. This oral NOEL with a dermal absorption factor of 5% should be used **only for non-cancer** dermal risk assessments. Dermal exposure **should not be** combined with inhalation exposure since a Long-Term inhalation risk assessment is not required.
This risk assessment is required.

(B). Carcinogenic Effects. The Q_1* of 4.39×10^{-2} should be used for estimating carcinogenic risk from occupational exposure. The dermal and inhalation exposures **should be combined** and appropriate dermal (5%) and inhalation (100%) absorption factors should be used in **carcinogenic** risk assessments.

5. Inhalation Exposure (Short and Intermediate-Term ONLY)

Except for an acute inhalation toxicity study, the results of which place Iprodione in Toxicity Category IV (LC_{50} = 5.16 mg/L), no other studies are available via this route. The current use pattern (4 days/week up to several weeks) indicate a concern only for Short and Intermediate-Term but not for Long-Term exposures via this route. Therefore, the **HIARC selected the doses only for Short and Intermediate-Term inhalation exposure risk assessments.**

i. Short-Term Inhalation Exposure.

The Developmental NOEL of 20 mg/kg/day from the special rat developmental toxicity study (MRID No.44365001) was selected for short term inhalation risk assessment. This NOEL is based on decreased AGD in male fetuses at 120 mg/kg/day (LOEL). The inhalation exposure component (i.e., µg a.i/lb/day) using a 100% absorption rate (default value) should be *converted to* an *equivalent oral dose* (mg/kg/day). This converted oral dose should then be compared to the NOEL identified above. Inhalation exposure **should not be** combined with dermal exposure since a dermal risk assessment is not required. **This risk assessment is required**.

ii. Intermediate-Term Inhalation Exposure.

The NOEL=of 6.1 mg/kg/day from the rat combined Chronic Toxicity/Carcinogenicity - Rat (MRID Nos.43308201 & 43000501). This NOEL is based on histopathological lesions in the male reproductive system and effects on the adrenal glands in males at 12.4 and in females at 16.5 mg/kg/day (LOEL).

The inhalation unit exposure (in µg a.i/lb/day) should be *converted to* an *equivalent oral dose* (mg/kg/day) using a 100% absorption rate (default value). This converted oral dose should then be compared to the NOEL identified above. Inhalation exposure **should not be** combined with dermal exposure since a dermal risk assessment is not required.

iii. Long-Term Exposure.

The current use pattern does not indicate a concern for Long-Term exposure or risk. This risk assessment is **NOT** required.

D. Margin of Exposure for Occupational/Residential Exposures:

The appropriate target MOEs for occupational and residential exposures was determined at the April 7, 1998 OPP Division Directors Meeting subsequent to the FQPA Safety Factor Committee.
The FQPA factor of 3X does not apply to occupational exposure scenarios, but does apply to residential exposure scenarios.

E. Recommendation for Aggregate Exposure Risk Assessments

For **acute** aggregate exposure risk assessment, combine the high end exposure values from food + water and compare it to the oral NOEL to calculate the MOE or percent acute RfD.

For **short and intermediate** aggregate exposure risk assessment, combine the average exposure values from food + water together with the exposure from inhalation route (100% absorption) only and compare it to the oral NOELs to calculate the MOE (dermal risk assessments are not required for these exposure periods).

For **chronic** aggregate exposure risk assessment, combine the average exposure values from food + water together. There are no chronic residential use scenarios to include in this risk assessment.

The doses and toxicological endpoints selected for various exposure scenarios are summarized below.

Table 3. Summary of Toxicological Endpoints to be used for Risk Assessment.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	Developmental NOEL=20	Decreased anogenital distance in male pups.	Developmental- Rat
	UF=100, plus 3X for FQPA	**Acute FQPA RfD = 0.06 mg/kg/day**	
Chronic Dietary	NOEL=6.1	*Histopathological* lesions in the male reproductive system and the adrenal glands in both sexes.	Combined Chronic Toxicity/ Carcinogenicity -Rat
	UF=100, plus 3x for FQPA	**Chronic FQPA RfD = 0.02 mg/kg/day**	
Carcinogenicity (Dietary)	Q_1*= 4.39×10^{-2}	Iprodione is classified as a **"Likely"** human carcinogen with a low-dose extrapolation approach for human risk assessment.	
Short-Term (Dermal)	Not Applicable	No dermal or systemic toxicity seen at the Limit-Dose in a 21-day dermal toxicity study in rabbits. This risk assessment is not required.	
Intermediate-Term (Dermal)	Not Applicable	No dermal or systemic toxicity seen at the Limit-Dose in a 21-day dermal toxicity study in rabbits. This risk assessment is not required.	
Long-Term (Dermal)[a] **Non-Cancer**	Oral NOEL=6.1 UF = 300	Histopathological lesions in the male *reproductive system* and the adrenal glands in both sexes.	Combined Chronic Toxicity/ Carcinogenicity-Rat
Long-Term (Dermal)[a] **Cancer**	Q_1*= 4.39×10^{-2}	Iprodione is classified as a **"Likely"** human carcinogen with a low-dose extrapolation approach for human risk assessment.	
Short-Term (Inhalation)[a]	Oral Developmental NOEL=20 UF = 300	Decreased anogenital distance in male pups.	Developmental-Rat
Intermediate-Term (Inhalation)[a]	Oral NOEL=6.1 UF = 300	Histopathological lesions in the male reproductive system and the adrenal glands in both sexes.	Combined Chronic Toxicity/ Carcinogenicity-Rat
Long-Term (Inhalation)	Not Applicable	Based on the use pattern, there is no concern for exposure or risk. This risk assessment is not required.	

a = Appropriate route-to-route extrapolation should be performed (i.e., a dermal absorption factor of 5% and an inhalation absorption factor of 100% used for conversion to oral equivalent doses and then compared to the oral NOELs).

3. Occupational and Residential Exposure and Risk Assessment

a. Summary of Use Patterns and Formulations

At this time products containing Iprodione are intended for both homeowner and occupational uses. Occupational uses include commercial/industrial lawns, golf course turf, ornamental and/or shade trees, ornamental herbaceous plants, ornamental woody shrubs and vines, and food crops.

Homeowner uses include garden and orchard type food crops, turfgrass, ornamental shrubs, trees and woody vines and ornamental herbaceous plants (USEPA 1997b and c).

Type of pesticide/target pests

Iprodione, 3-(3,5-Dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide, is a broad spectrum fungicide used to prevent, treat and control diseases on turfgrass, trees, ornamental flowering and foliage plants and food crop plants. Examples of the type of fungi that Iprodione is used to prevent, treat, and control include (but are not limited to) the following (USEPA 1997c):

- Dollar spot (Lanzia spp. and Moellerodiscus spp.), Brown patch (Rhizoctonia solani), Leaf spot and Melting out (Drechslera spp.) , Fusarium blight (Fusarium spp.), Gray snow mold (Typhula spp.) and Pink snow mold (Fusarium nivale), Corticum red thread (Laetisaria fuciformis) on turfgrass;
- Aerial web blight (Rhizoctonia sp.), Alternaria leaf blight (Alternaria zinniae), Botrytis blight (Botrytis sp.), Ink spot (Drechslera iridis), Ray blight (Ascochyta chrysanthami), Tulip fire (Botrytis tulipae), and Fusarium corm rot (Fusarium oxysporum) on ornamentals;
- Damping-off (Rhizoctonia solani) on cotton;
- Sclerotinia blight (Sclerotinia minor) on peanuts;
- Sheath blight (Rhizoctonia solani), Brown spot (Bipolaris oryzai), Sheath spot (Rhizoctonia oryzae) and Narrow brown leaf spot (Cercospora oryzae) on rice;
- Brown rot blossom blight (Monilinia spp.), Fruit brown rot (Monilinia spp.), Shot hole (Stigmina carpophila), Scab (Ventura carpophila), and Cherry leaf spot (Blumeriella jaapii) on stone fruit;
- Bunch rot (Botrytis cinerea) on grapes;
- Gray mold (Botrytis cinerea), White mold (Sclerotinia sclerotiorum) on beans, Black leg (Leptosphaeria maculans) on broccoli, Alternaria blight (Alternaria dauci) and Black crown rot

(Alternaria radicina) on carrots. White rot (Sclerotium cepivorum) on garlic. Lettuce drop (Sclerotinia spp.) and Brown rot (Rhizoctonia solani) on lettuce, and Early blight (Alaternaria solani) and White mold (Sclerotinia sclerotiorum) on potatoes.

Formulation types and percent active ingredient

Iprodione is formulated as a technical product (95 percent active ingredient), a liquid soluble concentrate (14 and 41.6 percent active ingredient), a wettable powder (33.3 and 50 percent active ingredient), a dry flowable (50 percent active ingredient), a flowable concentrate (41.6 percent active ingredient), an emulsifiable concentrate (19.65, 23.3 and 50 percent active ingredient), and as a granular (1.02 and 1.3 percent active ingredient). Some wettable powder formulations are contained in water-soluble packaging (USEPA 1997b and c).

Registered use sites

i. Occupational-use sites.

Iprodione has been registered for occupational-use on commercial/industrial lawns, golf course turf, ornamentals and shade trees, ornamental herbaceous plants, ornamental woody shrubs and vines, and food crops. The occupational crops use sites have been grouped as follows:

- **Agricultural Crops**, including almonds, apricots, cherries, nectarines, peaches, pecans, plums, prunes, beans (dried, lima, and snap), blackberries, blueberries, broccoli, bushberries, caneberries, carrots, garlic, grapes, ginseng, gooseberries, huckleberries, lettuce (head and leaf), loganberries, mustard cabbage, Chinese cabbage, dry bulb onions, peanuts, potatoes, raspberries, and strawberries.

- **Ornamentals**, including flowering trees and shrubs, woody shrubs and vines, evergreens, flowering and nonflowering plants, ground covers and shade trees.

- **Turfgrass,** including sod farms, golf courses and institutional lawn areas of bentgrass, blue grass, Bermuda grass, St. Augustine grass, rye grass, fine fescue or tall fescue.

ii. Non-occupational-use sites.

Potential residential and non-occupational use sites may include residential sites (e.g., exposure to fungicide use on fruit and vegetable gardens, ornamentals, and turfgrass), professional uses at residential sites (e.g., fungicide use on trees, shrubs, and other ornamentals, application to lawns), and other sites where non-occupational exposure may occur (e.g., turfgrass in golf courses, parks, residential and recreational areas). The non-occupational crops use sites have been grouped as follows:

- **Fruit/Nut Trees,** including almonds, apricots, cherries, nectarines, peaches, and plums.

- **Small Fruit/Vegetable Garden Crops,** including beans (dried, lima, and snap), blackberries, blueberries, broccoli, bushberries, caneberries, carrots, garlic, grapes, ginseng, gooseberries, huckleberries, lettuce (head and leaf), loganberries, mustard cabbage, Chinese cabbage, dry bulb onions, peanuts, potatoes, raspberries, and strawberries.

- **Ornamentals at Residences**, including shade trees, evergreens and flowering and non-flowering shrubs.

- **Turfgrass,** including residential lawn areas.

Application Rates (USEPA 1997b and c)

- **Commercial Agricultural Crops:** The maximum application rate for commercial crops ranges from 0.5 lb ai/acre to 1.0 lb ai/acre for all application methods.

- **Commercial Ornamentals:** The maximum application rate for pre-planting and cold storage dip treatments ranges from 0.005 to 0.01 lb ai/gallon. The maximum application rate for other application methods applicable to greenhouse treatments range from 0.002 to 0.01 lb ai/gallon. The maximum rates for field nursery application range from 1.4 to 4 lb ai/acre.

- **Commercial/Residential Turfgrass:** Using granular, dry flowable and liquid formulations, the maximum application rate applied to sod farms, golf courses and institutional and residential lawns ranged from 1.4 to 5.5 lb ai/acre. Granular formulations are to be applied using a light rate (1.4 lb ai/acre) to prevent certain fungi such as pink or gray snow mold or leaf spot. A normal (2.7 lb ai/acre) to heavy application rate (4.1 lb ai/acre) is recommended to control fungi such as leaf spot, brown patch and red leaf spot (EPA Reg. No. 538-159).

- **Residential Fruit and Nut Trees:** The maximum application rates range from 0.0013 to 0.0026 lb ai/gallon for foliar spray to fruit/nut trees.

- **Residential Fruit/Vegetable Garden Crops:** The maximum application rate ranges from 0.0052 to 0.104 lb ai/gallon.

- **Ornamentals at Residences:** The maximum applications rates vary from 0.002 to 0.01 lb ai/gallon.

Methods and Types of Equipment used for Mixing, Loading, and Application (USEPA 1997 b and c)

- **Commercial Agricultural Crops:** Equipment includes aircraft (fixed-wing and helicopter), airblast sprayer for orchards, chemigation, groundboom, drench, in furrow spray planter, and high pressure handwand. Seeds can be treated in slurry form or in a seed soaker. Additionally, a dip treatment may be used before cold storage or as a pre-planting preventive measure on strawberries.

- **Commercial Ornamentals:** Equipment used on nursery and green house stock includes high pressure handwand, low pressure handwand, backpack sprayer, chemigation systems, groundboom spray, drench and low pressure/high volume handgun. Additionally, a dip treatment may be used before cold storage or as a pre-planting preventive measure on certain ornamental stock, including roses, gladiolus and azaleas.

- **Commercial/Residential Turfgrass:** Granular application to turfgrass areas involves the use of a tractor-drawn spreader, belly grinder, push type lawn spreader, or hand application of granules for spot treatment. Liquid and wettable powder formulations can be applied to turfgrass sod farms, using chemigation systems, aircraft (fixed-wing or helicopter), groundbooms, low pressure/high volume handguns, low pressure handwands, high pressure handwands, and backpack sprayers. These same formulations can be applied to other turf areas such as institutional areas, golf courses and residential lawns

- **Residential Fruit and Nut Trees:** Equipment for residential application includes backpack sprayers, low pressure handwands, and garden hose-end sprayers.

- **Residential Fruit/Vegetable Garden Crops:** Equipment for residential application includes low pressure handwands, backpack sprayers, garden hose-end sprayers. Other possible application methods include dipping for cold storage or pre planting and seed soaking.

- **Ornamentals at Residences:** Ornamentals may be treated using a low pressure handwand, backpack sprayer, or a garden hose-end sprayer.

Timing and Frequency of Applications (USEPA 1997 b and c):

- **Commercial Agricultural Crops:** The maximum number of applications per season applied to commercial agricultural crops ranges from 1 (e.g., dip, in furrow spray at planting, post harvest spray to fruit, and seed soak or treatment) to 10 per season for crops such as carrots, dry bulb onions, and strawberries. Typically, the applications made 10 times per season (e.g., strawberries) are applied using one half the application rate of that for sites where the maximum number of applications is 4 times per year. Application intervals range from 7-21 days.

- **Commercial Ornamentals:** Foliar spray applications to ornamental crops can be sprayed to runoff at 7-14 day intervals for an unspecified maximum number of applications per season. Dip treatments to bare root roses, cuttings prior to planting, and corms prior to storage are applied only once per season. Drench treatments at seeding and/or after transplanting can be made at 14 day intervals.

- **Commercial/Residential Turfgrass:** Iprodione labels state that applications to turfgrass may be made at 7-30 day intervals an unspecified number of times per season, or as stated on some labels "as required"(e.g., EPA Reg. No. 264-562).

- **Residential Fruit and Nut Trees**: Iprodione labels call for a maximum of 5 applications per season at intervals of 7-14 days for stone fruit trees (e.g. apricots, nectarines, cherries, peaches, plums and prunes). A maximum of 4 applications per year can be made to almond trees at pink bud and if conditions are favorable for disease development, up to 3 subsequent applications can be made at: 1) full bloom, 2) petal fall, and 3) up to 5 weeks after petal fall.

- **Residential Fruit/Vegetable Garden Crops:** A maximum of 10 applications can be made to strawberries and dry bulb onions at 7-14 day intervals. The maximum number of applications per season for other vegetables ranges from 2 (e.g., broccoli and beans) to 4 (e.g., potatoes, carrots and caneberries), all applied at 7-14 day intervals.

- **Ornamentals at Residences**: Residential rate frequency and application intervals are the same as for commercial ornamental applications.

b. Applicator, Mixer, Loader (Handler) Exposure Assumptions & Risk Assessment

1. Occupational Exposures & Risks

EPA has determined, based on current use patterns, that there are potential exposures to workers handling Iprodione products, as well as to workers who come into contact with treated surfaces following applications of Iprodione products.

a. Handler Exposures & Risks

EPA has determined that there are potential exposures to mixers, loaders, applicators, or other handlers during usual use-patterns associated with Iprodione.

i. Handler Exposure Scenarios

Based on the use patterns, 19 major handler exposure scenarios were identified for Iprodione:

(1a) mixing, loading liquids for aerial/chemigation application; (1b) mixing, loading liquids for groundboom application; (1c) mixing, loading liquids for orchard airblast sprayer application; (1d) mixing, loading liquids for professional application to turfgrass/ornamentals using a low pressure/high volume handgun; (2a) mixing, loading wettable powder for aerial/chemigation application; (2b) mixing, loading wettable powder for groundboom application; (2c) mixing, loading wettable powder for orchard airblast sprayer application; (2d) mixing, loading wettable powder for professional applicator to turfgrass/ornamentals using a low pressure/high volume handgun; (3a) mixing, loading dry flowables for chemigation application; (3b) mixing, loading dry flowables for groundboom application; (4) loading granulars for tractor-drawn spreader application;(5) applying

sprays with fixed-wing aircraft; (6) applying sprays with a helicopter; (7) applying sprays using a groundboom sprayer; (8) applying to orchards with an airblast sprayer; (9) applying with a low pressure/high volume handgun to turfgrass/ornamentals; (10) applying granulars with a tractor-drawn spreader; (11) mixing, loading, applying sprays using a low pressure hand wand; (12) mixing, loading, applying sprays using a high pressure hand wand (13) mixing, loading, applying sprays using a backpack sprayer; (14) loading/ applying granulars using a belly grinder; (15) loading/ applying granulars with a push-type granular spreader; (16) mixing, loading, applying as a seed soak treatment; (17) mixing, loading, applying as a commercial seed treatment in slurry form; (18) mixing, loading, applying solutions as a dip treatment; and (19) flagging during aerial spray application.

ii. Handler Exposure Scenarios -- Data and Assumptions

No chemical-specific handler exposure data were submitted in support of the Reregistration of Iprodione. Therefore, an exposure assessment was developed for scenarios where appropriate surrogate data are available, using the *Pesticide Handlers Exposure Database (PHED) Version 1.1* (USEPA 1997d). Table 4 summarizes the caveats and parameters specific to the surrogate data used for each scenario and corresponding exposure/risk assessment. These caveats include the source of the data and an assessment of the overall quality of the data. The assessment of data quality is based on the number of observations and the available quality control data. The quality control data are based on a grading criteria established by the PHED task force.

The following assumptions and factors were used in order to complete this exposure assessment:

- Average body weight of an adult handler is 70 kg. This body weight is used in the intermediate-term inhalation and cancer assessments. A body weight of 60 kg is used in the short-term inhalation assessment because the NOEL is based on a developmental effect.

- Average work day interval represents an 8 hour workday (e.g., the acres treated or volume of spray solution prepared in a typical day).

- Daily acres and volumes (as appropriate) to be treated in each scenario. These are based on the ORE Science Advisory Council estimates of areas treated per day for the broad categories of application methods and equipment considered. They include:

    - -- 350 acres for aerial and chemigation applications in agricultural settings and to turfgrass (including flaggers supporting aerial applications)
    - -- 80 acres for groundboom spraying of agricultural areas, sod farms, and ornamental field stock
    - -- 80 acres for tractor-drawn spreader application to turfgrass
    - -- 40 acres for orchard airblast application
    - -- 5 acres for application to turfgrass using a low pressure/high volume handgun and to turf and ornamentals with a low pressure handwand and to turf with a high pressure handwand
    - -- 5 acres for application of granular formulations to turfgrass using a push-type spreader or belly grinder (e.g., golf courses)

-- 40 gallons of spray to turf and ornamentals using a low pressure handwand or backpack sprayer
-- 1,000 gallons of spray to ornamentals using a high pressure handwand

- For drench treatments no PHED data were available; thus, as a surrogate, the PHED unit exposure data for groundboom spray was used to calculate dermal and inhalation exposure.

- Calculations are completed at the maximum application rates for specific crops recommended by the available Iprodione labels to bracket risk levels associated with the various use patterns. No data were provided concerning the "typical" application rates used for Iprodione.

- Due to a lack of scenario-specific data, HED often must calculate unit exposure values using generic protection factors (PF) to represent various risk mitigation options (i.e., the use of personal protective equipment (PPE) and engineering controls). PPE protection factors include those representing a double layer of clothing (50 percent PF for body exposure), chemical resistant gloves (90 percent PF for hand exposure), and respiratory protection (80 percent PF for use of dust/mist mask). Engineering controls are generally assigned a PF of 80 percent.

iii. Handler Exposure and Non-Cancer Risk Estimates

Handler exposure assessments are completed by EPA using a baseline exposure scenario and, if required, increasing levels of risk mitigation (PPE and engineering controls) to achieve an acceptable margin of exposure (assumed to be MOE 100 or greater) or cancer risk (1.0E-4 to 1.0E-6 for workers). The baseline scenario generally represents a handler wearing long pants, a long-sleeved shirt, and no chemical-resistant gloves. The following tables present exposure and risk estimates for the handling of Iprodione. Table 5 presents the short-term and intermediate-term inhalation risks at baseline. Table 6 presents the PPE-level risks for those scenarios where MOEs are less than 100 at baseline. Table 7 presents the short-term and intermediate-term inhalation risks for water soluble bag formulations and applications employing closed cockpit aircraft.

In calculations of short-term and intermediate-term inhalation risks, potential daily exposures were calculated using the following formula:

$$\textit{Daily Inhalation Exposure}\left(\frac{mg\ ai}{day}\right) =$$
$$\textit{Unit Exposure}\left(\frac{\mu g\ ai}{lb\ ai}\right) \times \textit{Conversion Factor}\left(\frac{1mg}{1{,}000\ \mu g}\right) \times \textit{Use Rate}\left(\frac{lb\ ai}{A}\right) \times \textit{Daily Acres Treated}\left(\frac{A}{day}\right)$$

The potential baseline short-term and intermediate-term inhalation doses were calculated using the following formulas:

$$\text{Short-term Daily Inhalation Dose}\left(\frac{\text{mg ai}}{\text{kg/day}}\right) = \text{Short-term Daily Inhalation Exposure}\left(\frac{\text{mg ai}}{\text{day}}\right) \times \left(\frac{1}{\text{Body Weight (kg)}}\right)$$

$$\text{Intermediate-term Daily Inhalation Dose}\left(\frac{\text{mg ai}}{\text{kg/day}}\right) = \text{Intermediate-term Daily Inhalation Exposure}\left(\frac{\text{mg ai}}{\text{day}}\right) \times \left(\frac{1}{\text{Body Weight (kg)}}\right)$$

For Iprodione, the short-term inhalation dose was calculated using a 60 kg body weight, while the intermediate-term inhalation dose uses a 70 kg body weight in the calculations. An inhalation absorption rate of 100 percent was used in the calculations.

The baseline short-term and intermediate-term inhalation MOEs were calculated using the following formulas:

$$\text{Short-term Inhalation MOE} = \frac{\text{Short-term NOEL}\left(\frac{\text{mg}}{\text{kg/day}}\right)}{\text{Short-term Inhalation Daily Dose}\left(\frac{\text{mg}}{\text{kg/day}}\right)}$$

$$\text{Intermediate-term Inhalation MOE} = \frac{\text{Intermediate-term NOEL}\left(\frac{\text{mg}}{\text{kg/day}}\right)}{\text{Intermediate-term Inhalation Daily Dose}\left(\frac{\text{mg}}{\text{kg/day}}\right)}$$

For Iprodione, the short-term inhalation MOE was calculated using a NOEL of 20 mg/kg/day, and the intermediate-term inhalation MOE was calculated using a NOEL of 6.1 mg/kg/day.

Table 4. Exposure Scenario Descriptions for the Use of Iprodione

Exposure Scenario (Number)	Data Source	Standard Assumptions[a] (8-hr work day)	Comments[b]
Mixer/Loader Descriptors			
Mixing/Loading Liquid Formulations (1a/1b/1c/1d)	PHED V1.1	350 acres for aerial, 350 acres for chemigation of sod farms and agriculture, 100 acres for chemigation of ornamental nurseries, 80 acres for groundboom in agriculture, ornamental nurseries and turfgrass. 40 acres for orchard airblast applications and 5 acres for treatment of ornamentals and turf when using a low pressure/high volume handgun	**Baseline:** Hand, dermal, and inhalation = AB grades. Hand = 53 replicates; Dermal = 72 to 122 replicates; and Inhalation = 85 replicates. High confidence in hand, dermal and inhalation data. No protection factor was needed to define the unit exposure value. **PPE:** The same dermal data are used as for the baseline coupled with a 50% protection factor to account for an additional layer of clothing. A 5-fold PF (e.g. 80% PF was applied to the baseline inhalation data to account for the use of a dust mist respirator. Hands = AB grades. Hands = 59 replicates. High confidence in hands, dermal data. **Engineering Controls:** Mechanical transfer method. Hands, dermal and inhalation unit exposures = AB grades. Hands = 31 replicates; dermal = 16 to 22 replicates, and inhalation = 27 replicates. High confidence in dermal, hand and inhalation data. Gloves were worn during the use of the engineering controls.
Mixing/Loading Wettable Powders(2a/2b/2c/2d)	PHED V1.1	350 acres for aerial and chemigation of agriculture, 80 acres for groundboom in agriculture, 40 acres for orchard airblast applications	**Baseline:** Hands, dermal and inhalation = ABC grades. Hands = 7 replicates, dermal = 22-45 replicates and inhalation = 44 replicates. Low confidence in dermal, hands data due to the low number of hand replicates. Medium confidence in inhalation data. **PPE**: Gloved data for hands = ABC grades. Hands = 24 replicates. Medium confidence in hands data. Dermal values calculated by applying a 50% protection factor to baseline values to account for an additional layer of clothing. A 5-fold PF (e.g. 80% PF was applied to the baseline inhalation data). **Engineering Controls**: Water soluble bags. Dermal and hand data = AB grades. Inhalation = All grade. Inhalation = 15 replicates, dermal = 6-15 replicates and hands = 5 replicates. Low confidence in the dermal, hands and inhalation data.

Table 4. Exposure Scenario Descriptions for the Use of Iprodione (Continued)

Exposure Scenario (Number)	Data Source	Standard Assumptions[a] (8-hr work day)	Comments[b]
Mixing/Loading Dry Flowable Formulations (3a and 3b)	PHED V1.1	350 acres for chemigation of turfgrass, 80 acres for groundboom application to ornamentals, turfgrass and tractor-drawn spreader application to turfgrass	**Baseline:** Hands, dermal and inhalation = AB grades. Low confidence in hands, dermal data. High confidence in inhalation data. Hand = 7 replicates, dermal = 16-26 replicates and inhalation = 23 replicates. **PPE:** *Gloved data for hands = AB grade. High confidence in hands data.* Hands = 21 replicates. Dermal values calculated by applying a 50% protection factor to baseline values to account for an additional layer of clothing. A 5-fold PF (e.g. 80% PF was applied to the baseline inhalation data. **Engineering Controls:** Based on scenario for wettable powders (water soluble bags). See above scenario.
Loading Granular Formulations (4)	PHED V1.1	80 acres for tractor drawn *spreaders for turfgrass*	**Baseline:** Hands = All grade, dermal = ABC grade, and inhalation = AB *grade. Hands = 10 replicates; dermal = 33 to 78 replicates; and inhalation = 58 replicates. Low confidence in dermal/ hand data. High confidence in* inhalation data. **PPE:** Hands = AB grade, dermal = ABC grade. Hand = 45 replicates, dermal = 12-59 replicates. Low confidence in dermal and hands data. A 5-fold PF was applied to the baseline inhalation data to account for the use of a dust mist respirator. **Engineering Controls:** *Lock 'n load scenario. 98% PF was applied to baseline* data.
Applicator Descriptors			
Applying Sprays with a Fixed-Wing Aircraft (5)	PHED V1.1	350 acres for aerial	**Baseline:** No data **PPE:** No data **Engineering Controls:** Hands = AB grade, dermal and inhalation = ABC grade. Medium confidence in hands/dermal and inhalation data. Hands = 34 replicates, dermal = 24-48 replicates, and inhalation = 23 replicates.

Table 4. Exposure Scenario Descriptions for the Use of Iprodione (Continued)

Exposure Scenario (Number)	Data Source	Standard Assumptions[a] (8-hr work day)	Comments[b]
Applying Sprays with a Helicopter (6)	PHED V1.1	350 acres for aerial	**Baseline:** No data **PPE:** No data **Engineering Controls:** Hands and inhalation = A grade, dermal = C grade. Low confidence in inhalation data, and extremely low confidence in hands and dermal data due to very low number of replicates. Hands = 2 replicates, dermal = 3 replicates, and inhalation = 3 replicates.
Applying Sprays with a Groundboom Sprayer (7)	PHED V1.1	80 acres in agricultural, ornamental and turfgrass settings	**Baseline:** Hand, dermal, and inhalation = AB grades. Hands = 29 replicates, dermal = 23 to 42 replicates, and inhalation = 22 replicates. High confidence in hand, dermal, and inhalation data. **PPE:** The same dermal and inhalation data are used as for the baseline coupled with a 50% protection factor to account for an additional layer of clothing, and an 80% PF to account for the use of a dust mist respirator, respectively. Hands data are ABC grades with 21 replicates. Medium confidence in hands, and dermal data. **Engineering Controls:** Hands and dermal = ABC grade, inhalation = AB grade. Hands = 16 replicates, dermal = 20-31 replicates, inhalation = 16 replicates. Medium confidence in hands and dermal data, and high confidence in inhalation data.

Table 4. Exposure Scenario Descriptions for the Use of Iprodione (Continued)

Exposure Scenario (Number)	Data Source	Standard Assumptions[a] (8-hr work day)	Comments[b]
Applying to Orchards with an Airblast Sprayer (8)	PHED V1.1	40 acres for orchard spraying	**Baseline:** Hand, dermal and inhalation are AB grade. Hands 22 replicates, dermal = 32 to 49 replicates, and inhalation = 47 replicates. High confidence in hand, dermal and inhalation data. **PPE:** Hands and dermal = AB grade. Hands = 18 replicates, dermal = 31-48 replicates. High confidence in hands and dermal data. A 5-fold (80% PF) was applied to baseline inhalation data to account for use of dust-mist respirator. **Engineering Controls:** Dermal = AB grade, inhalation = ABC grade. High confidence in dermal data; low confidence in inhalation data. Inhalation = 9 replicates, dermal = 20-30 replicates. A 90% PF was applied to gloved data to represent no gloved scenario.
Applying with a Low Pressure/High Volume Handgun to Turfgrass (9)	PHED V1.1	5 acres for turfgrass	**Baseline:** No hand data. See PPE. Inhalation data are AB grades with 14 replicates and low to medium confidence. **PPE:** Dermal and inhalation data are C grade with low confidence. Hands = 14 replicates; dermal = 0-14 replicates. 80% PF was applied to baseline inhalation data to account for use of dust/mist respirator. **Engineering Controls:** Not feasible.
Applying Granulars with a Tractor-Drawn Spreader (10)	PHED V1.1	80 acres for turfgrass	**Baseline:** Hands, dermal and inhalation = AB grades. Low confidence in hands, dermal and inhalation data. Hands = 5 replicates, dermal = 1-5 replicates and inhalation = 5 replicates. **PPE:** The same hand and dermal data are used as for the baseline coupled with a 90% PF to account for chemical resistant gloves, and a 50% PF to account for an additional layer of clothing, respectively. The same inhalation data are used as for the baseline coupled with an 80% PF to account for the use of a dust mist respirator. **Engineering Controls:** Hands, dermal and inhalation data are AB grades. Hands = 24 replicates, dermal = 27-30 replicates, and inhalation = 37 replicates. High confidence in hands, dermal and inhalation data.

Table 4. Exposure Scenario Descriptions for the Use of Iprodione (Continued)

Exposure Scenario (Number)	Data Source	Standard Assumptions[a] (8-hr work day)	Comments[b]
Mixer/Loader/Applicator Descriptors			
Mixing/Loading/Applying with a Low Pressure Handwand (11)	PHED V1.1	5 acres for turfgrass application and 40 gallons for turf and ornamental use	**Baseline:** Dermal and inhalation = ABC grade, hands = All grades. Low confidence in hands/dermal data. Medium confidence in inhalation data. Hands = 70 replicates, dermal = 9-80 replicates and inhalation = 80 replicates. **PPE:** Hands = ABC grade with 10 replicates. Low confidence in dermal/hand data. The same dermal data are used as for the baseline coupled with a 50% protection factor to account for an additional layer of clothing . A 5-fold PF (e.g. 80% PF) was applied to the baseline inhalation data. **Engineering Controls:** Not feasible
Mixing/Loading/Applying with a High Pressure Handwand (12)	PHED V1.1	1,000 gallons for ornamentals and 5 acres for agricultural settings.	**Baseline:** Dermal = AB grades, inhalation = A grade. Dermal = 7-13 replicates; inhalation = 13 replicates. Gloved data was used to calculate the no gloved hand data, assuming gloves provide 90% protection. Hands = C grade with 13 replicates. Low confidence in hand, dermal, and inhalation data. Baseline data includes use of chemical-resistant gloves. **PPE:** The same dermal data are used as for the baseline coupled with a 50% protection factor to account for an additional layer of clothing. Hands data = C grade with 13 replicates. Low confidence in hand and dermal data. A 5-fold PF (e.g. 80% PF) was applied to the baseline inhalation data. **Engineering Controls:** Not feasible
Mixing/Loading/Applying with a Backpack Sprayer (13)	PHED V1.1	5 acres for turf use, and 40 gallons for turf and ornamental use	**Baseline:** No hands data. See PPE. Inhalation = A grade, with 11 replicates and low confidence. **PPE:** Dermal = AB grades. Hands = C grade. Dermal = 9-11 replicates, hands = 11 replicates. 80% PF was applied to baseline inhalation data to account for use of dust mist respirator. **Engineering Controls:** Not feasible.

Table 4. Exposure Scenario Descriptions for the Use of Iprodione (Continued)

Exposure Scenario (Number)	Data Source	Standard Assumptions[a] (8-hr work day)	Comments[b]
Loading/Applying Granulars Using a Belly Grinder (14)	PHED V1.1	5 acres for turfgrass application	**Baseline:** Hands and dermal = ABC grades and inhalation = AB grade. Medium confidence in hands/dermal data and high confidence in inhalation data. Hands = 23 replicates, dermal = 29-45 replicates and inhalation = 40 replicates. **PPE:** = Gloved data for hands = All grades with 20 replicates. Low confidence in hand data. The dermal data are taken from the baseline coupled with a 50% protection factor to account for an additional layer of clothing. A 5-fold protection factor (80% PF) was applied to baseline inhalation data to account for use of dust mist respirator. **Engineering Controls:** Not feasible
Loading/Applying Using a Push-Type Granular Spreader (15)	PHED V1.1	5 acres for turfgrass application	**Baseline:** Hand and dermal = C grades, and inhalation = B grade. Hand = 15 replicates, dermal = 0-15 replicates, and inhalation = 15 replicates. Low confidence in hand and dermal data, and high confidence in inhalation data. **PPE:** The same dermal and hand data are used as for the baseline coupled with a 50% protection factor to account for an additional layer of clothing and a 90% protection factor to account for the use of chemical resistant gloves. A 5-fold protection factor (80% PF) was applied to the inhalation data to account for use of dust mist respirator. **Engineering Controls:** Not feasible.
Mixing/Loading/Applying as a Seed Soak Treatment (16)	PHED V1.1	No Data	No Data
Mixing/Loading/Applying as a Commercial Seed Treatment in Slurry Form (17)	PHED V1.1	No Data	No Data
Mixing/Loading/Applying Solution as a Dip Treatment(18)	PHED V1.1	No Data	No Data

Exposure Scenario (Number)	Data Source	Standard Assumptions[a] (8-hr work day)	Comments[b]
Flagging Spray Applications (19)	PHED V1.1	350 acres	**Baseline:** Hands, dermal and inhalation data = AB grades. High confidence in dermal, hands and inhalation. Hands = 30 replicates, Inhalation = 28 replicates, and dermal = 18-28 replicates. **PPE:** Dermal and hands = AB grade. Hands = 30 replicates, dermal = 18-28 replicates. High confidence for dermal and hands data. A 80% PF was applied to baseline data to represent dust mist respirator. **Engineering Controls:** Hands and dermal = AB grade, inhalation = AB grade. Inhalation = 28 replicates, hand = 30 replicates, and dermal = 18-28 replicates. High confidence in hands, dermal data, and high confidence in inhalation data. These data are based on a 98% PF for enclosed truck.

[a] All *Standard Assumptions* are based on an 8-hour work day as estimated by HED.

[b] All handler exposure assessments in this document are based on the "Best Available" data as defined by the PHED SOP for meeting Subdivision U Guidelines (i.e., completing exposure assessments). Best available grades are assigned to data as follows: matrices with A and B grade data (i.e., Acceptable Grade Data) and a minimum of 15 replicates; if not available, then grades A, B and C data and a minimum of 15 replicates; if not available, then all data regardless of the quality (i.e., All Grade Data) and number of replicates. High quality data with a protection factor take precedence over low quality data with no protection factor. Generic data confidence categories are assigned as follows:

High = grades A and B and 15 or more replicates per body part
Medium = grades A, B, and C and 15 or more replicates per body part
Low = any run that included D or E grade data or has less than 15 replicates per body part.

Table 5. Occupational Short-term and Intermediate-term Inhalation Risks from Iprodione at Baseline

Exposure Scenario (Scen. #)	Baseline Inhalation Unit Exposure[a] (µg/lb ai)	Range of Application Rates[b] (lb ai/A)	Crop Type or Target[c]	Amount Handled per Day[d]	Baseline Daily Inhalation Exposure[e] (mg/day)	Short-term Baseline Daily Inhalation Dose[f] (mg/kg/day)	Int.-term Baseline Daily Inhalation Dose[g] (mg/kg/day)	Baseline Short-term Inhalation MOE[h] (mg/day)	Baseline Int.-term Inhalation MOE[i] (mg/day)
Mixer/Loader Risk									
Mixing/Loading Liquids for Aerial/Chemigation Application (1a)	1.2	0.5 lb ai/A	Ag	350 acres	0.21	0.0035	0.0030	5,700	2,000
		1 lb ai/A			0.42	0.0070	0.0060	2,900	1,000
		5.5 lb ai/A	Turf		2.3	0.038	0.033	530	180
		1.4 lb ai/A	Ornamentals	100 acres	0.17	0.0028	0.0024	7,100	2,500
Mixing/Loading Liquids for Groundboom Application (1b)	1.2	0.27 lb ai/A	Ag	80 acres	0.026	0.00043	0.00037	47,000	16,000
		0.5 lb ai/A			0.048	0.00080	0.00069	25,000	8,800
		1 lb ai/A			0.096	0.0016	0.0014	13,000	4,400
		1.4 lb ai/A	Ornamentals	80 acres	0.13	0.0022	0.0019	9,100	3,200
		4 lb ai/A			0.38	0.0063	0.0054	3,200	1,100
		5.5 lb ai/A	Turf		0.53	0.0088	0.0076	2,300	800
Mixing/Loading Liquid for Orchard Airblast Sprayer Application (1c)	1.2	0.5 lb ai/A	Ag	40 acres	0.024	0.00040	0.00034	50,000	18,000
		1 lb ai/A			0.048	0.00080	0.00069	25,000	8,800
Mixing/Loading Liquids for Professional Application to Turf Using a Low Pressure/High Volume Handgun (1d)	1.2	1.4 lb ai/A	Ornamentals	5 acres	0.0084	0.00014	0.00012	140,000	51,000
		5.5 lb ai/A	Turf		0.033	0.00055	0.00047	36,000	13,000
Mixing/Loading Wettable Powder for Aerial/Chemigation Application (2a)	43	0.5 lb ai/A	Ag	350 acres	7.5	0.13	0.11	150	55
		1 lb ai/A			15.0	0.25	0.21	80	29
Mixing/Loading Wettable Powder for Groundboom Application (2b)	43	0.5 lb ai/A	Ag	80 acres	1.7	0.028	0.024	710	250
		1 lb ai/A			3.4	0.057	0.049	350	120
Mixing/Loading Wettable Powder for Orchard Airblast Sprayer Application (2c)	43	0.5 lb ai/A	Ag	40 acres	0.86	0.014	0.012	1,400	510
		1 lb ai/A			1.7	0.028	0.024	710	250

Table 5. Occupational Short-term and Intermediate-term Inhalation Risks from Iprodione at Baseline (Continued)

Exposure Scenario (Scen. #)	Baseline Inhalation Unit Exposure[a] (µg/lb ai)	Range of Application Rates[b] (lb ai/A)	Crop Type or Target[c]	Amount Handled per Day[d]	Baseline Daily Inhalation Exposure[e] (mg/day)	Short-term Baseline Daily Inhalation Dose[f] (mg/kg/day)	Int.-term Baseline Daily Inhalation Dose[g] (mg/kg/day)	Baseline Short-term Inhalation MOE[h] (mg/day)	Baseline Int. term Inhalation MOE[i] (mg/day)
Mixing/Loading Wettable Powder for Professional Application to Turf using a Low pressure/High Volume Handgun (2d)	43	1.4 lb ai/A	*Ornamental*	5 acres	0.30	0.0050	0.0043	4,000	1,400
		5.5 lb ai/A	Turf		1.2	0.020	0.017	1,000	360
Mixing/Loading Dry Flowable for Chemigation Application (3a)	0.77	5.5 lb ai/A	Turf	350 acres	1.5	0.025	0.021	800	290
Mixing/Loading Dry Flowable Groundboom Application (3b)	0.77	1 lb ai/A	Ornamentals	80 *acres*	0.062	0.0010	0.00089	20,000	6,900
		5.5 lb ai/A	Turf	80 acres	0.34	0.0057	0.0049	3,500	1,200
Loading Granulars for Tractor-Drawn Spreader Application (4)	1.7	0.68 lb ai/A	Turf	80 acres	0.092	0.0015	0.0013	13,000	4,700
		1.4 lb ai/A			0.19	0.0032	0.0027	6,300	2,300
		4.1 lb ai/A			0.56	0.0093	0.0080	2,200	760
Applicator Exposure									
Applying Sprays with a Fixed-Wing Aircraft (5)	No Data See Eng. Con.	0.5 lb ai/A	Ag	350 acres	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.
		1 lb ai/A			See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.
Applying Sprays with a Helicopter (6)	No Data See Eng. Con.	0.5 lb ai/A	Ag	350 acres	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.
		1 lb ai/A			See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.
Applying Sprays with a Groundboom Sprayer (7)	0.74	*0.27 lb ai/A*	Ag	80 acres	*0.016*	*0.00027*	*0.00023*	74,000	27,000
		0.5 lb ai/A			0.030	0.00050	0.00043	40,000	14,000
		1 lb ai/A			0.059	0.00098	0.00084	20,000	7,300
		1.4 lb ai/A	Ornamentals	80 acres	0.083	0.0014	0.0012	14,000	5,100
		4 lb ai/A			0.24	0.0040	0.0034	5,000	1,800
		5.5 lb ai/A	Turf	80 *acres*	0.33	0.0055	0.0047	3,600	1,300

Table 5. Occupational Short-term and Intermediate-term Inhalation Risks from Iprodione at Baseline (Continued)

Exposure Scenario (Scen. #)	Baseline Inhalation Unit Exposure[a] (µg/lb ai)	Range of Application Rates[b] (lb ai/A)	Crop Type or Target[c]	Amount Handled per Day[d]	Baseline Daily Inhalation Exposure[e] (mg/day)	Short-term Baseline Daily Inhalation Dose[f] (mg/kg/day)	Int.-term Baseline Daily Inhalation Dose[g] (mg/kg/day)	Baseline Short-term Inhalation MOE[h] (mg/day)	Baseline Int. term Inhalation MOE[i] (mg/day)
Applying to Orchards with an Airblast Sprayer (8)	4.5	0.5 lb ai/A	Ag	40 acres	0.090	0.0015	0.0013	13,000	4,700
		1 lb ai/A			0.18	0.0030	0.0026	6,700	2,300
Applying with a Low Pressure/High Volume Handgun to Turfgrass (9)	1.4	1.4 lb ai/A	Ornamentals	5 acres	0.0098	0.00016	0.00014	120,000	44,000
		5.5 lb ai/A	Turf		0.039	0.00064	0.00055	31,000	11,000
Applying Granulars with a Tractor-Drawn Spreader (10)	1.2	0.68 lb ai/A	Turf	80 acres	0.065	0.0011	0.00093	18,000	6,600
		1.4 lb ai/A			0.13	0.0022	0.0019	9,100	3,200
		4.1 lb ai/A			0.39	0.0065	0.0056	3,100	1,100
Mixer/Loader/Applicator Exposure									
Mixing/Loading/Applying Sprays with a Low Pressure Handwand (11)	30	0.002 lb ai/gal	Turf & Ornamentals	40 gallons	0.0024	0.000040	0.000034	500,000	180,000
		0.01 lb ai/gal			0.012	0.00020	0.00017	100,000	36,000
		5.5 lb ai/A	Turf	5 acres	0.83	0.014	0.012	1,400	510
Mixing/Loading/Applying Sprays with a High Pressure Handwand (12)	120	0.5 lb ai/A	Ag	5 acres	0.30	0.0050	0.0043	4,000	1,400
		1 lb ai/A			0.60	0.010	0.0086	2,000	710
		0.002 lb ai/gal	Ornamentals	1,000 gallons	0.24	0.0040	0.0034	5,000	1,800
		0.01 lb ai/gal			1.2	0.020	0.017	1,000	360
Mixing/Loading/Applying Using a Backpack Sprayer (13)	30	0.002 lb ai/gal	Turf & Ornamentals	40 gallons	0.0024	0.000040	0.000034	500,000	180,000
		0.01 lb ai/gal			0.012	0.00020	0.00017	100,000	36,000
		5.5 lb ai/A	Turf	5 acres	0.83	0.014	0.012	1,400	510
Loading/Applying Granulars Using a Belly Grinder (14)	62	0.68 lb ai/A	Turf	5 acres	0.21	0.0035	0.0030	5,700	2,000
		1.4 lb ai/A			0.43	0.0072	0.0061	2,800	1,000
		4.1 lb ai/A			1.3	0.022	0.019	910	320

Table 5. Occupational Short-term and Intermediate-term Inhalation Risks from Iprodione at Baseline (Continued)

Exposure Scenario (Scen. #)	Baseline Inhalation Unit Exposure[a] (μg/lb ai)	Range of Application Rates[b] (lb ai/A)	Crop Type or Target[c]	Amount Handled per Day[d]	Baseline Daily Inhalation Exposure[e] (mg/day)	Short-term Baseline Daily Inhalation Dose[f] (mg/kg/day)	Int.-term Baseline Daily Inhalation Dose[g] (mg/kg/day)	Baseline Short-term Inhalation MOE[h] (mg/day)	Baseline Int. term Inhalation MOE[i] (mg/day)
Loading/Applying Using a Push-Type Granular Spreader (15)	6.3	0.68 lb ai/A	Turf	5 acres	0.0021	0.000035	0.000030	57,000	20,000
		1.4 lb ai/A			0.044	0.00073	0.00063	27,000	9,700
		4.1 lb ai/A			0.13	0.0022	0.0019	9,100	3,200
Mixing/Loading/Applying as a Seed Soak Treatment (16)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Mixing/Loading/Applying as a Commercial Seed Treatment in Slurry Form (17)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Mixing/Loading/Applying Solution as a Dip Treatment (18)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Flagger Exposure									
Flagging Spray Applications (19)	0.35	0.5 lb ai/A	Ag	350 acres	0.061	0.0010	0.00087	20,000	7,000
		1 lb ai/A			0.12	0.0020	0.0017	10,000	3,600

Footnotes:

a Baseline inhalation unit exposure reflects no respiratory protection.

b Application rates come from values found in the LUIS report and on Iprodione labels. For some scenarios, a range of application rates is used to represent different crops. For example:
(1) 0.27 lb ai/A applies to the in-furrow spray treatment of cotton during planting (EPA Reg. No. 264-482, 264-453).
(2) 0.5 lb ai/A applies to almonds, rice (aerial), Chinese mustard and dry bulb onions (EPA Reg. No. 264-482, 264-520).
(3) 1 lb ai/A applies to stone fruits, potatoes, peanuts, broccoli, lettuce and carrots (EPA Reg. 264-482).

c Crop Type or Target provides a general description of the intended uses of various products containing Iprodione. Separate categories are presented because of the distinct differences in application rates and acres treated.
Ag = agricultural crops and *Turf* = turfgrass including sod-farms, institutional areas and golf courses. *Ornamentals* = includes greenhouse, field, landscape, and conifer nurseries.

d Amount Handled Per Day values are from the EPA estimates of acreage treated, or volume handled in a single day for each exposure scenario of concern based on the application method.

e Baseline Daily Inhalation Exposure (mg/day) = Unit Exposure (μg/lb ai) * (1 mg/1000 μg) Conversion * Application Rate (lb ai/A or lb ai/gallon) * Amount Handled Per Day (acres/day or gallons/day).

f Short-term Baseline Daily Inhalation Dose (mg/kg/day) = Baseline Daily Inhalation Exposure (mg/day) / 60 (Body Weight).

g Intermediate-term Baseline Daily Inhalation Dose (mg/kg/day) = Baseline Daily Inhalation Exposure (mg/day) / 70 (Body Weight).

h Baseline Short-term Inhalation MOE (mg/day) = NOEL (20 mg/kg/day) / Short-term Baseline Inhalation Dose (mg/kg/day).

i Baseline Intermediate-term Inhalation MOE (mg/day) = NOEL (6.1 mg/kg/day) / Intermediate-term Baseline Inhalation Dose (mg/kg/day).

ıble 6. Occupational Short-term and Intermediate-term Inhalation Risks from Iprodione with PPE
or Scenarios with MOE's <100 at Baseline)

Exposure Scenario (Scen. #)	PPE Inhalation Unit Exposure[a] (μg/lb ai)	Range of Application Rates[b] (lb ai/A)	Crop Type or Target[c]	Amount Handled per Day[d]	PPE Daily Inhalation Exposure[e] (mg/day)	Short-term PPE Daily Inhalation Dose[f] (mg/kg/day)	Int.-term PPE Daily Inhalation Dose[g] (mg/kg/day)	PPE Short-term Inhalation MOE[h] (mg/day)	PPE Int. term Inhalation MOE[i] (mg/day)
Mixer/Loader Risk									
Mixing/Loading Wettable Powder for Aerial/Chemigation Application (2a)	8.6	0.5 lb ai/A	Ag	350 acres	1.5	--	0.021	--	290
		1 lb ai/A			3.0	0.050	0.043	400	140

Footnotes:

a PPE Inhalation Unit Exposure values were calculated with a 5-fold protection factor (80% PF) applied to baseline PHED values. This reflects use of a dust mist respirator.

b Application Rates come from values found in the LUIS report and on Iprodione labels. For some scenarios, a range of application rates is used to represent different crops. For example:
(1) 0.27 lb ai/A applies to the in furrow spray treatment of cotton during planting (EPA Reg. No. 264-482, 264-453).
(2) 0.5 lb ai/A applies to almonds, rice (aerial), Chinese mustard and dry bulb onions (EPA Reg. No. 264-482, 264-520).
(3) 1 lb ai/A applies to stone fruits, potatoes, peanuts, broccoli, lettuce and carrots (EPA Reg. 264-482).

c Crop Type or Target provides a general description of the intended uses of various products containing Iprodione. Separate categories are presented because of the distinct differences in application rates and acres treated.
Ag = agricultural crops and *Turf* = turfgrass including sod-farms, institutional areas and golf courses. *Ornamentals* = includes greenhouse, field, landscape, and conifer nurseries.

d Amount Handled Per Day values are from the EPA estimates of acreage treated, or volume handled in a single day for each exposure scenario of concern based on the application method.

e PPE Daily Inhalation Exposure (mg/day) = Unit Exposure (μg/lb ai) * (1 mg/1000 μg) Conversion * Application Rate (lb ai/A or lb ai/gallon) * Amount Handled Per Day (acres/day or gallons/day).

f Short-term PPE Daily Inhalation Dose (mg/kg/day) = PPE Daily Inhalation Exposure (mg/day) / 60 (Body Weight).

g Intermediate-term PPE Daily Inhalation Dose (mg/kg/day) = PPE Daily Inhalation Exposure (mg/day) / 70 (Body Weight).

h PPE Short-term Inhalation MOE (mg/day) = NOEL (20 mg/kg/day) / Short-term PPE Inhalation Dose (mg/kg/day).

I PPE Intermediate-term Inhalation MOE (mg/day) = NOEL (6.1 mg/kg/day) / Intermediate-term PPE Inhalation Dose (mg/kg/day).

ble 7. Occupational Short-term and Intermediate-term Inhalation Risks from Iprodione with Engineering Controls - Water Soluble-Packets and closed Cab Aerial Application[k]

Exposure Scenario (Scen. #)	Range of Application Rates[a] (lb ai/A)	Crop Type or Target[b]	Amount Handled per Day[c]	Engineering Controls[i]				
				Inhalation Unit Exposure[d] (µg/lb ai)	Short-term Daily Inhalation Dose[e] (mg/kg/day)	Short-term MOE[f] (mg/day)	Int.-term Daily Inhalation Dose[g] (mg/kg/day)	Int.-term MOE[h] (mg/day)
Mixer/Loader Risk								
Mixing/Loading Wettable Powder for Aerial/Chemigation Application (2a)	0.5 lb ai/A	Ag	350 acres	0.24	0.00070	29,000	0.00060	10,000
	1 lb ai/A				0.0014	14,000	0.0012	5,100
Mixing/Loading Wettable Powder for Groundboom Application (2b)	0.5 lb ai/A	Ag	80 acres	0,24	0.00016	130,000	0.00014	44,000
	1 lb ai/A				0.00032	63,000	0.00027	23,000
Mixing/Loading Wettable Powder for Orchard Airblast Sprayer Application (2c)	0.5 lb ai/A	Ag	40 acres	0.24	0.000080	250,000	0.000069	88,000
	1 lb ai/A				0.00016	130,000	0.00014	44,000
Mixing/Loading Wettable Powder for Professional Application to Turfgrass using a Low Pressure/ High Volume Handgun (2d)	1.4 lb ai/A	ornamentals	5 acres	0.24	0.000028	710,000	0.000024	250,000
	5.5 lb ai/A	turf			0.00011	180,000	0.000094	65,000
Applicator Risk								
Applying Sprays with a Fixed-wing Aircraft (5)	0.5 lb ai/A	Ag	350 acres	0.068	0.00020	100,000	0.00017	36,000
	1 lb ai/A				0.00040	50,000	0.00034	18,000
Applying Sprays with a Helicopter (6)	*0.5 lb ai/A*	Ag	*350 acres*	*0.0018*	*0.0000053*	*3,800,000*	*0.0000045*	*1,400,000*
	1 lb ai/A				0.000011	1,800,000	0.0000090	680,000

Footnotes:

a Application rates come from values found in the LUIS report and on Iprodione labels. For some scenarios, a range of application rates is used to represent different crops. For example:
(1) 0.27 lb ai/A applies to the in furrow spray treatment of cotton during planting [EPA Reg. No. 264-482, 264-453].
(2) 0.5 lb ai/A applies to almonds, rice (aerial), Chinese mustard and dry bulb onions [EPA Reg. No. 264-482, 264-520].
(3) 1 lb ai/A applies to stone fruits, potatoes, peanuts, broccoli, lettuce and carrots [EPA Reg. 264-482].

b Crop Type or Target provides a general description of the intended uses of various products containing Iprodione. Separate categories are presented because of the distinct differences in application rates and acres treated.

c Amount Handled Per Day values are from the EPA estimates of acreage treated, or volume handled in a single day for each exposure scenario of concern based on the application method.

d Unit Exposure values are taken from PHED V1.1

e *Short-term Daily Inhalation Dose = Inhalation Unit Exposure (ug/lb ai) * Application Rate (lb ai/A) * Amount Handled per Day (acres/day)/Body Weight* (60 kg).

f Short-term MOE = NOEL (20 mg/kg/day)/Short-term Daily Inhalation Dose (mg/kg/day).

g Intermediate-term Daily Inhalation Dose = Inhalation Unit Exposure (ug/lb ai) * Application Rate (lb ai/A) * Amount Handled per Day (acres/day)/Body Weight (70 kg).

h *Intermediate-term* MOE = NOEL (6.1 *mg/kg/day)/Intermediate-term* Daily Inhalation Dose *(mg/kg/day).*

i Engineering Controls = 2a, 2b, 2c water soluble bags; 5,6 enclosed cockpit.

j This assessment includes assessments for those scenarios which are currently packaged or applied with engineering controls.

iv. Handler Exposure and Risk Estimates for Cancer

Handler exposure assessments were completed by EPA using a baseline exposure scenario and, as needed, increasing levels of risk mitigation (PPE and engineering controls) to achieve acceptable cancer risks. Tables 8, 9, and 10 present total cancer risk calculations at baseline, with PPE and with engineering controls, respectively, for each exposure scenario.

The calculations of daily dermal and inhalation exposure to Iprodione by handlers were used to calculate the daily dose, and hence the risks, to those handlers. Potential daily dermal exposure was calculated using the following formula:

$$\text{Daily Dermal Exposure}\left(\frac{mg\ ai}{day}\right) = \text{Unit Exposure}\left(\frac{mg\ ai}{lb\ ai}\right) \times \text{Use Rate}\left(\frac{lb\ ai}{A}\right) \times \text{Daily Acres Treated}\left(\frac{A}{day}\right)$$

Potential daily inhalation exposure was calculated using the following formula:

$$\text{Daily Inhalation Exposure}\left(\frac{mg\ ai}{day}\right) =$$
$$\text{Unit Exposure}\left(\frac{\mu g\ ai}{lb\ ai}\right) \times \text{Conversion Factor}\left(\frac{1mg}{1{,}000\ \mu g}\right) \times \text{Use Rate}\left(\frac{lb\ ai}{A}\right) \times \text{Daily Acres Treated}\left(\frac{A}{day}\right)$$

The daily dermal and inhalation doses were calculated using a 70 kg body weight using the following formulas:

$$\text{Daily Inhalation Dose}\left(\frac{mg\ ai}{kg/day}\right) = \text{Daily Inhalation Exposure}\left(\frac{mg\ ai}{day}\right) \times \left(\frac{1}{\text{Body Weight (kg)}}\right)$$

$$\text{Daily Dermal Dose}\left(\frac{mg\ ai}{Kg/Day}\right) = \text{Daily Dermal Exposure}\left(\frac{mg\ ai}{Day}\right) \times \left(\frac{1}{\text{Body Weight (Kg)}}\right) \times 0.05\ \text{Dermal Absorption Factor}$$

$$\text{Total Daily Dose} = \text{Daily Dermal Dose}\left(\frac{mg}{kg/day}\right) + \text{Daily Inhalation Dose}\left(\frac{mg}{kg/day}\right)$$

The lifetime average daily dose (LADD) was calculated using the following formula:

$$\text{LADD}\left(\frac{mg}{kg/day}\right) = \text{Daily Total Dose}\left(\frac{mg}{kg/day}\right) \times \left(\frac{\text{days worked}}{365\ \text{days per year}}\right) \times \left(\frac{35\ \text{years worked}}{70\ \text{year lifetime}}\right)$$

Total cancer risk was calculated using the following formula:

$$Total\ Cancer\ Risk = LADD \times Q1^*$$

where $Q_1^* = 4.39$ E-02

The following assumptions and factors were used in order to complete this cancer risk assessment:

- The average body weight of 70 kg is used, representing a typical adult (USEPA 1997, Exposure Factors Handbook).
- Exposure time is assumed to be 8 hours per day. This represents a typical work day.
- Exposure duration is assumed to be 35 years. This represents a typical working lifetime.
- Lifetime is assumed to be 70 years (USEPA 1997, Exposure Factors Handbook).
- Dermal absorption is assumed to be 5 percent, and inhalation absorption is assumed to be 100 percent (UISEPA 1997a, USEPA 1998). The doses were added together to represent total daily dose.
- The $Q1^*$ used in the cancer assessment was 4.39E-02.
- Two exposure frequencies were used in the calculations, the first represented the maximum number of applications per site per season to represent private use, and the second frequency applied a factor of 10 to the first frequency to represent commercial handlers making multiple applications per site per season. These are typical to high-end values.

ıble 8. Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Iprodione at Baseline

Exposure Scenario (Scen. #)	Baseline Dermal Unit Exposure[a] (mg/lb ai)	Baseline Inhalation Unit Exposure[b] (μg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	Daily Dermal Exposure[f] (mg/day)	Daily Inhalation Exposure[g] (mg/day)	Baseline Total Daily Dose (mg/kg/day)	Number of Exposures per Year[i]	Baseline LADD[j] (mg/kg/day)	Baseline Total Cancer Risk[k]
Mixer/Loader Risk											
Mixing/Loading Liquids for Aerial/Chemigation Application (1a)	2.9	1.2	0.5 lb ai/A	Ag	350 acres	510	0.21	0.37	10 / 100	5.1E-3 / 5.1E-2	2.2E-4 / 2.2E-3
			1 lb ai/A			1,000	0.42	0.73	4 / 40	4.0E-3 /4.0E-2	1.8E-4 / 1.8E-3
			5.5 lb ai/A	Turf		5,600	2.3	4.0	6 / 60	3.3E-2 / 3.3E-1	1.4E-3 / 1.4E-2
			1.4 lb ai/A	Ornamentals	100 acres	410	0.17	0.29	8 / 80	3.3E-3 / 3.3E-2	1.4E-4 / 1.4E-3
Mixing/Loading Liquids for Groundboom Application (1b)	2.9	1.2	0.27 lb ai/A	Ag	80 acres	63	0.026	0.045	1 / 10	6.2E-5 / 6.2E-4	2.7E-6 / 2.7E-5
			0.5 lb ai/A			120	0.048	0.084	10 / 100	1.2E-3 / 1.2E-2	5.3E-5 / 5.3E-4
			1 lb ai/A			230	0.096	0.17	10 / 100	2.3E-3 / 2.3E-2	1.0E-4 / 1.0E-3
			1.4 lb ai/A	Ornamentals	80 acres	320	0.13	0.23	8 / 80	2.5E-3 / 2.5E-2	1.1E-4 / 1.1E-3
			4 lb ai/A			930	0.38	0.67	8 / 80	7.3E-3 / 7.3E-2	3.2E-4 / 3.2E-3
			5.5 lb ai/A	Turf		1,300	0.53	0.92	8 / 80	1.0E-2 / 1.0E-1	4.4E-4 / 4.4E-3
Mixing/Loading Liquid for Orchard Airblast Sprayer Application (1c)	2.9	1.2	0.5 lb ai/A	Ag	40 acres	58	0.024	0.042	4 / 40	2.3E-4 / 2.3E-3	1.0E-5 / 1.0E-4
			1 lb ai/A			120	0.048	0.084	4 / 40	4.6E-4 / 4.6E-3	2.0E-5 / 2.0E-4
Mixing/Loading Liquids for Professional Application to Turf Using a Low Pressure/High Volume Handgun (1d)	2.9	1.2	1.4 lb ai/A	Ornamentals	5 acres	20	0.0084	0.015	8 / 80	1.6E-4 / 1.6E-3	7.0E-6 / 7.0E-5
			5.5 lb ai/A	Turf		80	0.033	0.057	6 / 60	4.8E-4 / 4.8E-3	2.1E-5 / 2.1E-4
Mixing/Loading Wettable Powder for Aerial/Chemigation Application (2a)	3.7	43	0.5 lb ai/A	Ag	350 acres	650	7.5	0.57	10 / 100	7.8E-3 / 7.8E-2	3.4E-4 / 3.4E-3
			1 lb ai/A			1,300	15	1.1	4 / 40	6.0E-3 / 6.0E-2	2.6E-4 / 2.6E-3
Mixing/Loading Wettable Powder for Groundboomt Application (2b)	3.7	43	0.5 lb ai/A	Ag	80 acres	150	1.7	0.13	10 / 100	1.8E-3 / 1.8E-2	7.9E-5 / 7.9E-4
			1 lb ai/A			300	3.4	0.26	5 / 50	1.8E-3 / 1.8E-2	7.9E-5 / 7.9E-4
Mixing/Loading Wettable Powder for Orchard Airblast Sprayer Application (2c)	3.7	43	0.5 lb ai/A	Ag	40 acres	74	0.86	0.065	4 / 40	3.6E-4 / 3.6E-3	1.6E-5 / 1.6E-4
			1 lb ai/A			150	1.7	0.13	4 / 40	7.1E-4 / 7.1E-3	3.1E-5 / 3.1E-4

Table 8. Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Iprodione at Baseline (Continued)

Exposure Scenario (Scen. #)	Baseline Dermal Unit Exposure[a] (mg/lb ai)	Baseline Inhalation Unit Exposure[b] (μg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	Daily Dermal Exposure[f] (mg/day)	Daily Inhalation Exposure[g] (mg/day)	Baseline Total Daily Dose (mg/kg/day)	Number of Exposures per Year[i]	Baseline LADD[j] (mg/kg/day)	Baseline Total Cancer Risk[k]
Mixing/Loading Wettable Powder for Professional Application to Turf using a Low Pressure/High Volume Handgun (2d)	3.7	43	1.4 lb ai/A	Ornamentals	5 acres	26	0.30	0.023	8 / 80	2.5 E-4 / 2.5 E-3	1 1 E-5 / 1 1 E-4
			5.5 lb ai/A	Turf		100	1.2	0.90	6 / 60	7.4 E-4 / 7.4 E-3	3 2 E-5 / 3 2 E-4
Mixing/Loading Dry Flowable for Chemigation Application (3a)	*0.066*	*0.77*	*5.5 lb ai/A*	*Turf*	*350 acres*	*130*	*1.5*	*0.11*	*6 / 60*	*9.0E-4 / 9.0E-3*	*4 0E-5 / 4 0 E-4*
Mixing/Loading Dry Flowable Groundboom Application (3b)	0.066	0.77	1 lb ai/A	Ornamentals	80 acres	5.3	0.062	0.0047	8 / 80	5.2E-5 /5.2E-4	2.3E-6 / 2.3E-5
			5.5 lb ai/A	Turf	80 acres	29	0.34	0.026	8 / 80	2.9E-4 / 2.9E-3	1.3E-5 / 1.3E-4
Loading Granulars for Tractor-Drawn Spreader Application (4)	0.0084	1.7	0.68 lb ai/A	Turf	80 acres	0.46	0.093	0.0016	8 / 80	1.8E-5 / 1.8E-4	7 9E-7 / 7 9E-6
			1.4 lb ai/A			0.94	0.19	0.0034	8 / 80	3 7E-5 / 3.7E-4	1 6E-6 / 1 6E-5
			4.1 lb ai/A			2.8	0.56	0.0099	8 / 80	1 1E-4 / 1.1E-3	4 8E-6 / 4 8E-5
Applicator Risk											
Applying Sprays with a Fixed-Wing Aircraft (5)	No Data See EC	No Data See EC	0.5 lb ai/A	Ag	350 acres	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.
			1 lb ai/A			See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.
Applying Sprays with a Helicopter (6)	No Data See EC	No Data See EC	0.5 lb ai/A	Ag	350 acres	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.
			1 lb ai/A			See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.
Applying Sprays with a Groundboom Sprayer (7)	0.014	0.74	0.27 lb ai/A	Ag	80 acres	0.30	0.016	4.4E-4	1 / 10	6.0E-7 / 6.0E-6	2 6E-8 / 2 6E-7
			0.5 lb ai/A			0.56	0.030	8.2E-4	10 / 100	1.1E-5 / 1.1E-4	4 8E-7 / 4 8E-6
			1 lb ai/A			1.1	0.059	0.0016	10 / 100	2.2E-5 / 2.2E-4	9 7E-7 / 9 7E-6
			1.4 lb ai/A	Ornamentals	80 acres	1.6	0.083	0.0023	8 / 80	2.5E-5 / 2.5E-4	1 1E-6 / 1 1E-5
			4 lb ai/A			4.5	0.24	0.0066	8 / 80	7.2E-5 / 7.2E-4	3 2E-6 / 3 2E-5
			5.5 lb ai/A	*Turf*	*80 acres*	6.2	*0.33*	*0.0091*	*8 / 80*	1.0E-4 / 1.0E-3	4 4E-6 / 4 4E-5

Table 8. Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Iprodione at Baseline (Continued)

Exposure Scenario (Scen. #)	Baseline Dermal Unit Exposure[a] (mg/lb ai)	Baseline Inhalation Unit Exposure[b] (μg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	Daily Dermal Exposure[f] (mg/day)	Daily Inhalation Exposure[g] (mg/day)	Baseline Total Daily Dose (mg/kg/day)	Number of Exposures per Year[h]	Baseline LADD[i] (mg/kg/day)	Baseline Total Cancer Risk[j]
Applying to Orchards with an Airblast Sprayer (8)	0.36	4.5	0.5 lb ai/A	Ag	40 acres	7.2	0.090	0.0064	4 / 40	3.5E-5 / 3.5E-4	1.5E-6 / 1.5E-5
			1 lb ai/A			14	0.18	0.013	4 / 40	7.1E-5 / 7.1E-4	3.1E-6 / 3.1E-5
Applying with a Low Pressure/High Volume Handgun to Turfgrass (9)[k]	No Data (See PPE)	1.4	1.4 lb ai/A	Ornamentals	5 acres	NA	0.098	NA	8 / 80	NA	NA
			5.5 lb ai/A	Turf		NA	0.038	NA	8 / 80	NA	NA
Applying Granulars with a Tractor-Drawn Spreader (10)	0.0099	1.2	0.68 lb ai/A	Turf	80 acres	0.54	0.065	0.0013	8 / 80	1.4E-5 / 1.4E-4	6.1E-7 / 6.1E-6
			1.4 lb ai/A			1.1	0.13	0.0027	8 / 80	3.0E-5 / 3.0E-4	1.3E-6 / 1.3E-5
			4.1 lb ai/A			3.2	0.39	0.0079	8 / 80	8.7E-5 / 8.7E-4	3.8E-6 / 3.8E-5
Mixer/Loader/Applicator Exposure											
Mixing/Loading/Applying Sprays with a Low Pressure Handwand (11)	100	30	0.002 lb ai/gal	Turf & Ornamentals	40 gallons	8.0	0.0024	0.0057	8 / 80	6.3E-5 / 6.3E-4	2.8E-6 / 2.8E-5
			0.01 lb ai/gal			40	0.012	0.029	8 / 80	3.2E-4 / 3.2E-3	1.4E-5 / 1.4E-4
			5.5 lb ai/A	Turf	5 acres	2,800	0.83	2.0	8 / 80	2.2E-2 / 2.2E-1	9.7E-4 / 9.7E-3
Mixing/Loading/Applying Sprays with a High Pressure Handwand (12)	3.5	120	0.5 lb ai/A	Ag	5 acres	8.8	0.30	0.011	10 / 100	1.5E-4 / 1.5E-3	6.6E-6 / 6.6E-5
			1 lb ai/A			18	0.60	0.021	10 / 100	2.9E-4 / 2.9E-3	1.3E-5 / 1.3E-4
			0.002 lb ai/gal	Ornamentals	1,000 gallons	7.0	0.24	0.0084	8 / 80	9.2E-5 / 9.2E-4	4.0E-6 / 4.0E-5
			0.01 lb ai/gal			35	1.2	0.042	8 / 80	4.6E-4 / 4.6E-3	2.0E-5 / 2.0E-4
Mixing/Loading/Applying Using a Backpack Sprayer (13)	No Data See PPE	30	0.002 lb ai/gal	Turf & Ornamentals	40 gallons	See PPE	0.0024	See PPE	8 / 80	See PPE	See PPE
			0.01 lb ai/gal				0.012		8 / 80		
			5.5 lb ai/A	Turf	5 acres	See PPE	See PPE	See PPE	8 / 80	See PPE	See PPE

Table 8. Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Iprodione at Baseline (Continued)

Exposure Scenario (Scen. #)	Baseline Dermal Unit Exposure[a] (mg/lb ai)	Baseline Inhalation Unit Exposure[b] (μg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	Daily Dermal Exposure[f] (mg/day)	Daily Inhalation Exposure[g] (mg/day)	Baseline Total Daily Dose (mg/kg/day)	Number of Exposures per Year[i]	Baseline LADD[j] (mg/kg/day)	Baseline Total Cancer Risk[k]
Loading/Applying Granulars Using a Belly Grinder (14)	10	62	0.68 lb ai/A	Turf	5 acres	34	0.21	0.027	8 / 80	3.0E-4 / 3.0E-3	1.3E-5 / 1.3E-4
			1.4 lb ai/A			70	0.43	0.056	8 / 80	6.1E-4 / 6.1E-3	2.7E-5 / 2.7E-4
			4.1 lb ai/A			210	1.3	0.16	8 / 80	1.8E-3 / 1.8E-2	7.9E-5 / 7.9E-4
Loading/Applying Using a Push-Type Granular Spreader (15)	2.9	6.3	0.68 lb ai/A	Turf	5 acres	9.9	0.021	0.0073	8 / 80	8.0E-5 / 8.0E-4	3.5E-6 / 3.5E-5
			1.4 lb ai/A			20	0.044	0.015	8 / 80	1.6E-4 / 1.6E-5	7.2E-6 / 7.2E-5
			4.1 lb ai/A			59	0.13	0.044	8 / 80	4.8E-4 / 4.8E-3	2.1E-5 / 2.1E-4
Mixing/Loading/Applying as a Seed Soak Treatment (16)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Mixing/Loading/Applying as a Commercial Seed Treatment in Slurry Form (17)	*No Data*	*No Data*	*No Data*	*No Data*	*No Data*	*No Data*	*No Data*	*No Data*	*No Data*	*No Data*	*No Data*
Mixing/Loading/Applying Solution as a Dip Treatment (18)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Flagger Risk											
Flagging Spray Applications (19)	0.011	0.35	0.5 lb ai/A	Ag	350 acres	1.8	0.061	0.0021	10 / 100	2.9E-5 / 2.9E-4	1.3E-6 / 1.3E-5
			1 lb ai/A			3.5	0.12	0.0042	4 / 40	2.3E-5 / 2.3E-4	1.0E-6 / 1.0E-5

Table 8. Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Iprodione at Baseline (Continued)

Footnotes:

a Baseline Dermal Unit Exposure represents long pants, long sleeved shirt, no gloves, open mixing/loading, and open cab tractors as appropriate.

b Baseline Inhalation Unit Exposure reflects no respiratory protection.

c Application rates come from values found in the LUIS report and on Iprodione labels. For some scenarios, a range of application rates is used to represent different crops. For example:
(1) 0.27 lb ai/A applies to the in furrow spray treatment of cotton during planting [EPA Reg. No. 264-482, 264-453].
(2) 0.5 lb ai/A applies to almonds, rice (aerial), Chinese mustard and dry bulb onions [EPA Reg. No. 264-482, 264-520].
(3) 1 lb ai/A applies to stone fruits, potatoes, peanuts, broccoli, lettuce and carrots [EPA Reg. 264-482].

d Crop Type or Target provides a general description of the intended uses of various products containing Iprodione. Separate categories are presented because of the distinct differences in application rates and acres treated.
Ag = agricultural crops and *Turf* = turfgrass including sod-farms, institutional areas and golf courses. *Ornamentals* = includes greenhouse, field, landscape, and conifer nurseries.

e Amount Handled Per Day values are from the EPA estimates of acreage treated, or volume handled in a single day for each exposure scenario of concern based on the application method.

f Daily Dermal Exposure (mg/day) = Unit Exposure (mg/lb ai) * Application Rate (lb ai/A or lb ai/gallon) * Amount Handled Per Day (acres/day or gallons/day).

g Daily Inhalation Exposure (mg/day) = Unit Exposure (µg/lb ai) * (1 mg/1000 µg) Conversion * Application Rate (lb ai/A or lb ai/gallon) * Amount Handled Per Day (acres/day or gallons/day).

h Baseline Total Daily Dose = [Baseline Daily Dermal Exposure (mg/day) * 0.05 (Dermal Absorption Factor) + Baseline Daily Inhalation Exposure (mg/day)]/Body Weight (70 kg).

l Number of Exposures Per Year is based on maximum number of applications which represent private use. A factor of 10 was used to estimate commercial use.

j Baseline LADD (mg/kg/day) = Baseline Total Daily Dose (mg/kg/day) * (Number of days exposure per year /365 days per year) * 35 years worked/70 year lifetime.

k Baseline Total Cancer Risk = Baseline LADD (mg/kg/day) * (Q_1*), where Q_1* = 4.39E-2 (mg/kg/day).

l Baseline dermal data not available. See PPE for dermal and combined exposures, doses, and risks.

ble 9. Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Iprodione with PPE

Exposure Scenario (Scen. #)	PPE Dermal Unit Exposure[a] (mg/lb ai)	PPE Inhalation Unit Exposure[b] (μg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	PPE Daily Dermal Exposure[f] (mg/day)	PPE Daily Inhalation Exposure[g] (mg/day)	PPE Total Daily Dose (mg/kg/day)[h]	Number of Exposures per Year[i]	PPE LADD[j] (mg/kg/day)	PPE Total Cancer Risk[k]
Mixer/Loader Risk											
Mixing/Loading Liquids for Aerial/Chemigation Application (1a)	0.017	0.24	0.5 lb ai/A	Ag	350 acres	3.0	0.042	0.0027	10 / 100	3.7E-5 / 3.7E-4	1.6E-6 / 1.6E-5
			1 lb ai/A			6.0	0.084	0.0055	4 / 40	3.0E-5 / 3.0E-4	1.3E-6 / 1.3E-5
			5.5 lb ai/A	Turf		33	0.46	0.030	6 / 60	2.5E-4 / 2.5E-3	1.1E-5 / 1.1E-4
			1.4 lb ai/A	Ornamentals	100 acres	2.4	0.034	0.0022	8 / 80	2.4E-5 / 2.4E-4	1.1E-6 / 1.1E-5
Mixing/Loading Liquids for Groundboom Application (1b)	0.017	0.24	0.27 lb ai/A	Ag	80 acres	0.37	0.0052	0.00034	1 / 10	4.7E-7 / 4.7E-6	2.1E-8 / 2.1E-7
			0.5 lb ai/A			0.68	0.0096	0.00062	10 / 100	8.5E-6 / 8.5E-5	3.7E-7 / 3.7E-6
			1 lb ai/A			1.4	0.019	0.0013	10 / 100	1.8E-5 / 1.8E-4	7.9E-7 / 7.9E-6
			1.4 lb ai/A	Ornamentals	80 acres	1.9	0.027	0.0017	8 / 80	1.9E-5 / 1.9E-4	8.3E-7 / 8.3E-6
			4 lb ai/A			5.4	0.077	0.0050	8 / 80	5.5E-5 / 5.5E-4	2.4E-6 / 2.4E-5
			5.5 lb ai/A	Turf		7.5	0.11	0.0069	8 / 80	7.6E-5 / 7.6E-4	3.3E-6 / 3.3E-5
Mixing/Loading Liquid for Orchard Airblast Sprayer Application (1c)	0.017	0.24	0.5 lb ai/A	Ag	40 acres	0.34	0.0048	0.00031	4 / 40	1.7E-6 / 1.7E-5	7.5E-8 / 7.5E-7
			1 lb ai/A			0.68	0.0096	0.00062	4 / 40	3.4E-6 / 3.4E-5	1.5E-7 / 1.5E-6
Mixing/Loading Liquids for Professional Application to Turf Using a Low Pressure/High Volume Handgun (1d)	0.017	0.24	1.4 lb ai/A	Ornamentals	5 acres	0.12	0.0017	0.00011	8 / 80	1.2E-6 / 1.2E-5	5.3E-8 / 5.3E-7
			5.5 lb ai/A	Turf		0.47	0.0066	0.00043	6 / 60	3.5E-6 / 3.5E-5	1.5E-7 / 1.5E-6
Mixing/Loading Wettable Powder for Aerial/Chemigation Application (2a)	0.13	8.6	0.5 lb ai/A	Ag	350 acres	23	1.5	0.038	10 / 100	5.2E-4 / 5.2E-3	2.3E-5 / 2.3E-4
			1 lb ai/A			46	3.0	0.076	4 / 40	4.2E-4 / 4.2E-3	1.8E-5 / 1.8E-4
Mixing/Loading Wettable Powder for Groundboom Application (2b)	0.13	8.6	0.5 lb ai/A	Ag	80 acres	5.2	0.34	0.0086	10 / 100	1.2E-4 / 1.2E-3	5.3E-6 / 5.3E-5
			1 lb ai/A			10	0.69	0.017	5 / 50	1.2E-4 / 1.2E-3	5.3E-6 / 5.3E-5
Mixing/Loading Wettable Powder for Orchard Airblast Sprayer Application (2c)	0.13	8.6	0.5 lb ai/A	Ag	40 acres	2.6	0.17	0.0043	4 / 40	2.4E-5 / 2.4E-4	1.1E-6 / 1.1E-5
			1 lb ai/A			5.2	0.34	0.0086	4 / 40	4.7E-5 / 4.7E-4	2.1E-6 / 2.1E-5

Table 9. Combined Occupational Dermal and Inhalation Cancer Risk Assessment for Iprodione with PPE (Continued)

Exposure Scenario (Scen. #)	PPE Dermal Unit Exposure[a] (mg/lb ai)	PPE Inhalation Unit Exposure[b] (µg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	PPE Daily Dermal Exposure[f] (mg/day)	PPE Daily Inhalation Exposure[g] (mg/day)	PPE Total Daily Dose (mg/kg/day)[h]	Number of Exposures per Year[i]	PPE LADD[j] (mg/kg/day)	PPE Total Cancer Risk[k]
Mixing/Loading Wettable Powder for Professional Application to Turf using a Low Pressure/High Volume Handgun (2d)	0.13	8.6	1.4 lb ai/A	Ornamentals	5 acres	0.91	0.060	0.0015	8 / 80	1.7E-5 / 1.7E-4	7.3E-7 / 7.3E-6
			5.5 lb ai/A	turf		3.6	0.24	0.0059	6 / 60	4.9E-5 / 4.9E-4	2.1E-6 / 2.1E-5
Mixing/Loading Dry Flowable for Chemigation Application (3a)	0.047	0.15	5.5 lb ai/A	Turf	350 acres	90	0.29	0.068	6 / 60	5.6E-4 / 5.6E-3	2.5E-5 / 2.5E-4
Mixing/Loading Dry Flowable Groundboom Application (3b)	0.047	0.15	1 lb ai/A	Ornamentals	80 acres	3.8	0.012	0.0029	8 / 80	3.2E-5 / 3.2E-4	1.4E-6 / 1.4E-5
			5.5 lb ai/A	Turf	80 acres	21	0.066	0.016	8 / 80	1.8E-4 / 1.8E-3	7.9E-6 / 7.9E-5
Loading Granulars for Tractor-Drawn Spreader Application (4)	0.0034	0.34	0.68 lb ai/A	Turf	80 acres	0.18	0.018	0.00039	8 / 80	4.3E-6 / 4.3E-5	1.9E-7 / 1.9E-6
			1.4 lb ai/A			0.38	0.038	0.00081	8 / 80	8.9E-6 / 8.9E-5	3.9E-7 / 3.9E-6
			4.1 lb ai/A			1.1	0.11	0.0024	8 / 80	2.6E-5 / 2.6E-4	1.1E-6 / 1.1E-5
Applicator Risk											
Applying Sprays with a Fixed-Wing Aircraft (5)	No Data See Eng. Con.	No Data See Eng. Con.	0.5 lb ai/A	Ag	350 acres	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.
			1 lb ai/A								
Applying Sprays with a Helicopter (6)	No Data See Eng. Con.	No Data See Eng. Con.	0.5 lb ai/A	Ag	350 acres	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.	See Eng. Con.
			1 lb ai/A								
Applying Sprays with a Groundboom Sprayer (7)	0.011	0.15	0.27 lb ai/A	Ag	80 acres	0.24	0.0032	0.00022	1 / 10	3.0E-7 / 3.0E-6	1.3E-8 / 1.3E-7
			0.5 lb ai/A			0.44	0.0060	0.00040	10 / 100	5.5E-6 / 5.5E-5	2.4E-7 / 2.4E-6
			1 lb ai/A			0.88	0.012	0.00080	10 / 100	1.1E-5 / 1.1E-4	4.8E-7 / 4.8E-6
			1.4 lb ai/A	Ornamentals	80 acres	1.2	0.017	0.0011	8 / 80	1.2E-5 / 1.2E-4	5.3E-7 / 5.3E-6
			4 lb ai/A			3.5	0.048	0.0032	8 / 80	3.5E-5 / 3.5E-4	1.5E-6 / 1.5E-5
			5.5 lb ai/A	Turf	80 acres	4.8	0.066	0.0044	8 / 80	4.8E-5 / 4.8E-4	2.1E-6 / 2.1E-5
Applying to Orchards with an Airblast Sprayer (8)	0.22	0.90	0.5 lb ai/A	Ag	40 acres	4.4	0.018	0.0034	4 / 40	1.9E-5 / 1.9E-4	8.3E-7 / 8.3E-6
			1 lb ai/A			8.8	0.036	0.0068	4 / 40	3.7E-5 / 3.7E-4	1.6E-6 / 1.6E-5

Table 9. Combined Occupational Dermal and Inhalation Cancer Risk Assessment for Iprodione with PPE (Continued)

Exposure Scenario (Scen. #)	PPE Dermal Unit Exposure[a] (mg/lb ai)	PPE Inhalation Unit Exposure[b] (μg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	PPE Daily Dermal Exposure[f] (mg/day)	PPE Daily Inhalation Exposure[g] (mg/day)	PPE Total Daily Dose (mg/kg/day)[h]	Number of Exposures per Year[i]	PPE LADD[j] (mg/kg/day)	PPE Total Cancer Risk[k]
Applying with a Low Pressure/High Volume Handgun to Turfgrass (9)	0.19	0.28	1.4 lb ai/A	Ornamentals	5 acres	1.3	0.0020	0.0010	8 / 80	1.1E-5 / 1.1E-4	4.7E-7 / 4.7E-6
			5.5 lb ai/A	Turf		5.2	0.0077	0.0038	8 / 80	4.2E-5 / 4.2E-4	1.8E-6 / 1.8E-5
Applying Granulars with a Tractor-Drawn Spreader (10)	0.0042	0.24	0.68 lb ai/A	Turf	80 acres	0.23	0.013	0.00035	8 / 80	3.8E-6 / 3.8E-5	1.7E-7 / 1.7E-6
			1.4 lb ai/A			0.47	0.027	0.00072	8 / 80	7.9E-6 / 7.9E-5	3.5E-7 / 3.5E-6
			4.1 lb ai/A			1.4	0.079	0.0021	8 / 80	2.3E-5 / 2.3E-4	1.0E-6 / 1.0E-5
Mixer/Loader/Applicator Risk											
Mixing/Loading/Applying Sprays with a Low Pressure Handwand (11)	0.37	6	0.002 lb ai/gal	Turf & Ornamentals	40 gallons	0.03	0.00048	2.8E-5	8 / 80	3.1E-7 / 3.1E-6	1.4E-8 / 1.4E-7
			0.01 lb ai/gal			0.15	0.0024	0.00014	8 / 80	1.5E-6 / 1.5E-5	6.6E-8 / 6.6E-7
			5.5 lb ai/A	Turf	5 acres	10	0.17	0.0096	8 / 80	1.1E-4 / 1.1E-3	4.8E-6 / 4.8E-5
Mixing/Loading/Applying Sprays with a High Pressure Handwand (12)	1.6	24	0.5 lb ai/A	Ag	5 acres	4.0	0.060	0.0037	10 / 100	5.1E-5 / 5.1E-4	2.2E-6 / 2.2E-5
			1 lb ai/A			8.0	0.12	0.0074	10 / 100	1.0E-4 / 1.0E-3	4.4E-6 / 4.4E-5
			0.002 lb ai/gal	Ornamentals	1,000 gallons	3.2	0.048	0.0030	8 / 80	3.3E-5 / 3.3E-4	1.4E-6 / 1.4E-5
			0.01 lb ai/gal			16	0.24	0.015	8 / 80	1.6E-4 / 1.6E-3	7.0E-6 / 7.0E-5
Mixing/Loading/Applying Using a Backpack Sprayer (13)	1.6	6	0.002 lb ai/gal	Turf & Ornamentals	40 gallons	0.13	0.00048	0.00010	8 / 80	1.1E-6 / 1.1E-5	4.8E-8 / 4.8E-7
			0.01 lb ai/gal			0.64	0.0024	0.00049	8 / 80	5.4E-6 / 5.4E-5	2.4E-7 / 2.4E-6
			5.5 lb ai/A	Turf	5 acres	44	0.17	0.034	8 / 80	3.7E-4 / 3.7E-3	1.6E-5 / 1.6E-4
Loading/Applying Granulars Using a Belly Grinder (14)	9.3	12	0.68 lb ai/A	Turf	5 acres	28	0.041	0.021	8 / 80	2.2E-4 / 2.2E-3	9.9E-6 / 9.9E-5
			1.4 lb ai/A			57	0.084	0.042	8 / 80	4.6E-4 / 4.6E-3	2.0E-5 / 2.0E-4
			4.1 lb ai/A			170	0.25	0.12	8 / 80	1.4E-3 / 1.4E-2	5.9E-5 / 5.9E-4
Loading/Applying Using a Push-Type Granular Spreader (15)	0.73	1.3	0.68 lb ai/A	Turf	5 acres	2.5	0.0044	0.0018	8 / 80	2.0E-5 / 2.0E-4	8.8E-7 / 8.8E-6
			1.4 lb ai/A			5.1	0.0091	0.0038	8 / 80	4.2E-5 / 4.2E-4	1.8E-6 / 1.8E-5
			4.1 lb ai/A			15	0.027	0.011	8 / 80	1.2E-4 / 1.2E-3	5.3E-6 / 5.3E-5

Table 9. Combined Occupational Dermal and Inhalation Cancer Risk Assessment for Iprodione with PPE (Continued)

Exposure Scenario (Scen. #)	PPE Dermal Unit Exposure[a] (mg/lb ai)	PPE Inhalation Unit Exposure[b] (µg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	PPE Daily Dermal Exposure[f] (mg/day)	PPE Daily Inhalation Exposure[g] (mg/day)	PPE Total Daily Dose (mg/kg/day)[h]	Number of Exposures per Year[i]	PPE LADD[j] (mg/kg/day)	PPE Total Cancer Risk[k]
Mixing/Loading/Applying as a Seed Soak Treatment (16)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Mixing/Loading/Applying as a Commercial Seed Treatment in Slurry Form (17)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Mixing/Loading/Applying Solution as a Dip Treatment (18)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Flagger Risk											
Flagging Spray Applications (19)	0.01	0.07	0.5 lb ai/A	Ag	350 acres	1.8	0.012	0.0015	10 / 100	2.1E-5 / 2.1E-4	9.2E-7 / 9.2E-6
			1 lb ai/A			3.5	0.025	0.0029	4 / 40	1.6E-5 / 1.6E-4	7.0E-7 / 7.0E-6

Footnotes:

a PPE Dermal Unit Exposure represents double layer of clothes, and chemical resistant gloves.

b PPE Inhalation Unit Exposure reflects use of dust/mist respirator (5-fold PF).

c Application rates come from values found in the LUIS report and on Iprodione labels. See Table 7 for particular examples.

d Crop Type or Target provides a general description of the intended uses of various products containing Iprodione. Separate categories are presented because of the distinct differences in application rates and acres treated.
Ag = agricultural crops and *Turf* = turfgrass including sod-farms, institutional areas and golf courses. *Ornamentals* = includes greenhouse, field, landscape, and conifer nurseries.

e Amount Handled Per Day values are from the EPA estimates of acreage treated, or volume handled in a single day for each exposure scenario of concern based on the application method.

f PPE Daily Dermal Exposure (mg/day) = PPE Unit Exposure (mg/lb ai) * Application Rate (lb ai/A or lb ai/gallon) * Amount Handled Per Day (acres/day or gallons/day).

g PPE Daily Inhalation Exposure (mg/day) = PPE Unit Exposure (µg/lb ai) * (1 mg/1000 µg) Conversion * Application Rate (lb ai/A or lb ai/gallon) * Amount Handled Per Day (acres/day or gallons/day).

h PPE Total Daily Dose = [PPE Daily Dermal Exposure (mg/day) * 0.05 (Dermal Absorption Factor) + PPE Daily Inhalation Exposure (mg/day)]/Body Weight (70 kg).

i Number of Exposures Per Year is based on maximum number of applications which represent private use. A factor of *10* was used to estimate commercial use.

j PPE LADD (mg/kg/day) = PPE Total Daily Dose (mg/kg/day) * (Number of days exposure per year /365 days per year) * 35 years worked/70 year lifetime.

k PPE Total Cancer Risk = PPE LADD (mg/kg/day) * (Q_1*), where Q_1* = 4.39E-2 (mg/kg/day).

ble 10. Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Iprodione with Engineering Controls

Exposure Scenario (Scen. #)	Eng. Cont. Dermal Unit Exposure[a] (mg/lb ai)	Eng. Cont. Inhalation Unit Exposure[b] (µg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	Eng. Con. Daily Dermal Exposure[f] (mg/day)	Eng. Con. Daily Inhalation Exposure[g] (mg/day)	Eng. Cont. Total Daily Dose (mg/kg/day)[h]	Number of Exposures per Year[i]	Eng. Cont. LADD[j] (mg/kg/day)	Eng. Cont. Total Cancer Risk[k]
Mixer/Loader Risk											
Mixing/Loading Liquids for Aerial/Chemigation Application (1a)	0.0086	0.083	0.5 lb ai/A	Ag	350 acres	1.5	0.015	0.0013	10 / 100	1.8E-5 / 1.8E-4	7.9E-7 / 7.9E-6
			1 lb ai/A			3	0.029	0.0026	4 / 40	1.4E-5 / 1.4E-4	6.1E-7 / 6.1E-6
			5.5 lb ai/A	Turf		17	0.16	0.014	6 / 60	1.2E-4 / 1.2E-3	5.3E-6 / 5.3E-5
			1.4 lb ai/A	Ornamentals	100 acres	1.2	0.012	0.0010	8 / 80	1.1E-5 / 1.1E-4	4.8E-7 / 4.8E-6
Mixing/Loading Liquids for Groundboom Application (1b)	0.0086	0.083	0.27 lb ai/A	Ag	80 acres	0.19	0.0018	0.00016	1 / 10	2.2E-7 / 1.1E-6	9.7E-9 / 9.7E-8
			0.5 lb ai/A			0.34	0.0033	0.00029	10 / 100	4.0E-6 / 4.0E-5	1.8E-7 / 1.8E-6
			1 lb ai/A			0.69	0.0066	0.00059	10 / 100	8.1E-6 / 8.1E-5	3.6E-7 / 3.6E-6
			1.4 lb ai/A	Ornamentals	80 acres	0.96	0.0093	0.00082	8 / 80	9.0E-6 / 9.0E-5	4.0E-7 / 4.0E-6
			4 lb ai/A			2.8	0.027	0.0024	8 / 80	2.6E-5 / 2.6E-4	1.1E-6 / 1.1E-5
			5.5 lb ai/A	Turf		3.8	0.037	0.0032	8 / 80	3.5E-5 / 3.5E-4	1.5E-6 / 1.5E-5
Mixing/Loading Liquid for Orchard Airblast Sprayer Application (1c)	0.0086	0.083	0.5 lb ai/A	Ag	40 acres	0.17	0.0017	0.00015	4 / 40	8.2E-7 / 8.2E-6	3.6E-8 / 3.6E-7
			1 lb ai/A			0.34	0.0033	0.00029	4 / 40	1.6E-6 / 1.6E-5	7.0E-8 / 7.0E-7
Mixing/Loading Liquids for Professional Application to Turf Using a Low Pressure/High Volume Handgun (1d)	0.0086	0.083	1.4 lb ai/A	Ornamentals	5 acres	0.060	0.00058	0.000051	8 / 80	5.6E-7 / 5.6E-6	2.5E-8 / 2.5E-7
			5.5 lb ai/A	Turf		0.24	0.0023	0.00020	6 / 60	1.6E-6 / 1.6E-5	7.0E-8 / 7.0E-7
Mixing/Loading Wettable Powder for Aerial/Chemigation Application (2a)	0.021	0.24	0.5 lb ai/A	Ag	350 acres	3.7	0.042	0.0032	10 / 100	4.4E-5 / 4.4E-4	1.9E-6 / 1.9E-5
			1 lb ai/A			7.4	0.084	0.0065	4 / 40	3.5E-5 / 3.5E-4	1.6E-6 / 1.6E-5
Mixing/Loading Wettable Powder for Groundboomt Application (2b)	0.021	0.24	0.5 lb ai/A	Ag	80 acres	0.84	0.0096	0.00074	10 / 100	1.0E-5 / 1.0E-4	4.4E-7 / 4.4E-6
			1 lb ai/A			1.7	0.019	0.0015	5 / 50	1.0E-5 / 1.0E-4	4.4E-7 / 4.4E-6
Mixing/Loading Wettable Powder for Orchard Airblast Sprayer Application (2c)	0.021	0.24	0.5 lb ai/A	Ag	40 acres	0.42	0.0048	0.00037	4 / 40	2.0E-6 / 2.0E-5	8.9E-8 / 8.9E-7
			1 lb ai/A			0.84	0.0096	0.00074	4 / 40	4.0E-6 / 4.0E-5	1.8E-7 / 1.8E-6
Mixing/Loading Wettable Powder for Professional Application with Low Pressure/High Volume Handgun (2d)	0.021	0.24	1.4 lb ai/A	Ornamentals	5 acres	0.15	0.0017	0.00013	8 / 80	1.4E-6 / 1.4E-5	6.2E-8 / 6.2E-7
			5.5 lb ai/A	Turf		0.58	0.0066	0.00051	6 / 60	4.2E-6 / 4.2E-5	1.8E-7 / 1.8E-6

Table 10. Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Iprodione with Engineering Controls (Continued)

Exposure Scenario (Scen. #)	Eng. Cont. Dermal Unit Exposure[a] (mg/lb ai)	Eng. Cont. Inhalation Unit Exposure[b] (μg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	Eng. Con. Daily Dermal Exposure[f] (mg/day)	Eng. Con. Daily Inhalation Exposure[g] (mg/day)	Eng. Cont. Total Daily Dose (mg/kg/day)[h]	Number of Exposures per Year[i]	Eng. Cont. LADD[j] (mg/kg/day)	Eng. Cont. Total Cancer Risk[k]
Mixing/Loading Dry Flowable for Chemigation Application (3a)	0.021	0.24	5.5 lb ai/A	Turf	350 acres	40	0.46	0.035	6 / 60	2.9E-4 / 2.9E-3	1.3E-5 / 1.3E-4
Mixing/Loading Dry Flowable Groundboom Application (3b)	0.021	0.24	1 lb ai/A	Ornamentals	80 acres	1.7	0.019	0.0015	8 / 80	1.6E-5 / 1.6E-4	7.1E-7 / 7.1E-6
			5.5 lb ai/A	Turf	80 acres	9.2	0.11	0.0081	8 / 80	8.9E-5 / 8.9E-4	3.9E-6 / 3.9E-5
Loading Granulars for Tractor-Drawn Spreader Application (4)	0.00017	0.034	0.68 lb ai/A	Turf	80 acres	0.0092	0.0018	0.000032	8 / 80	3.5E-7 / 3.5E-6	1.5E-8 / 1.5E-7
			1.4 lb ai/A			0.019	0.0038	0.000068	8 / 80	7.5E-7 / 7.5E-6	3.3E-8 / 3.3E-7
			4.1 lb ai/A			0.056	0.011	0.00020	8 / 80	2.2E-6 / 2.2E-5	9.7E-8 / 9.7E-7
Applicator Risk											
Applying Sprays with a Fixed-Wing Aircraft (5)	0.0050	0.068	0.5 lb ai/A	Ag	350 acres	0.88	0.012	0.00080	10 / 100	1.1E-5 / 1.1E-4	4.8E-7 / 4.8E-6
			1 lb ai/A			1.8	0.024	0.0016	4 / 40	8.8E-6 / 8.8E-5	3.9E-7 / 3.9E-6
Applying Sprays with a Helicopter (6)	0.0019	0.0018	0.5 lb ai/A	Ag	350 acres	0.33	0.00032	0.00024	10 / 100	3.3E-6 / 3.3E-5	1.4E-7 / 1.4E-6
			1 lb ai/A			0.67	0.00063	0.00049	4 / 40	2.7E-6 / 2.7E-5	1.2E-7 / 1.2E-6
Applying Sprays with a Groundboom Sprayer (7)	0.005	0.043	0.27 lb ai/A	Ag	80 acres	0.11	0.00093	0.000092	1 / 10	1.3E-7 / 1.3E-6	5.7E-9 / 5.7E-8
			0.5 lb ai/A			0.20	0.0017	0.00017	10 / 100	2.3E-6 / 2.3E-5	1.0E-7 / 1.0E-6
			1 lb ai/A			0.40	0.0034	0.00033	10 / 100	4.5E-6 / 4.5E-5	2.0E-7 / 2.0E-6
			1.4 lb ai/A	Ornamentals	80 acres	0.56	0.0048	0.00047	8 / 80	5.2E-6 / 5.2E-5	2.3E-7 / 2.3E-6
			4 lb ai/A			1.6	0.014	0.0013	8 / 80	1.4E-5 / 1.4E-4	6.1E-7 / 6.1E-6
			5.5 lb ai/A	Turf	80 acres	2.2	0.019	0.0018	8 / 80	2.0E-5 / 2.0E-4	8.8E-7 / 8.8E-6
Applying to Orchards with an Airblast Sprayer (8)	0.019	0.45	0.5 lb ai/A	Ag	40 acres	0.38	0.0090	0.00040	4 / 40	2.2E-6 / 2.2E-5	9.6E-8 / 9.6E-7
			1 lb ai/A			0.76	0.018	0.00080	4 / 40	4.4E-6 / 4.4E-5	1.9E-7 / 1.9E-6
Applying with a Low Pressure/High Volume Handgun to Turfgrass (9)	NA	NA	1.4 lb ai/A	Ornamentals	5 acres	NA	NA	NA	8 / 80	NA	NA
			5.5 lb ai/A	Turf		NA	NA	NA	8 / 80	NA	NA

Table 10. Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Iprodione with Engineering Controls (Continued)

Exposure Scenario (Scen. #)	Eng. Cont. Dermal Unit Exposure[a] (mg/lb ai)	Eng. Cont. Inhalation Unit Exposure[b] (μg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	Eng. Con. Daily Dermal Exposure[f] (mg/day)	Eng. Con. Daily Inhalation Exposure[g] (mg/day)	Eng. Cont. Total Daily Dose (mg/kg/day)[h]	Number of Exposures per Year[i]	Eng. Cont. LADD[j] (mg/kg/day)	Eng. Cont. Total Cancer Risk[k]
Applying Granulars with a Tractor-Drawn Spreader (10)	0.0021	0.22	0.68 lb ai/A	Turf	80 acres	0.11	0.012	0.00025	8 / 80	2.7E-6 / 2.7E-5	1.2E-7 / 1.2E-6
			1.4 lb ai/A			0.24	0.025	0.00053	8 / 80	5.8E-6 / 5.8E-5	2.5E-7 / 2.5E-6
			4.1 lb ai/A			0.69	0.072	0.0015	8 / 80	1.6E-5 / 1.6E-4	7.0E-7 / 7.0E-6
Mixer/Loader/Applicator Exposure											
Mixing/Loading/Applying Sprays with a Low Pressure Handwand (11)	NA	NA	0.002 lb ai/gal	Turf & Ornamentals	40 gallons	NA	NA	NA	8 / 80	NA	NA
			0.01 lb ai/gal						8 / 80		
			5.5 lb ai/A	Turf	5 acres	NA	NA	NA	8 / 80	NA	NA
Mixing/Loading/Applying Sprays with a High Pressure Handwand (12)	NA	NA	0.5 lb ai/A	Ag	5 acres	NA	NA	NA	10 / 100	NA	NA
			1 lb ai/A						10 / 100		
			0.002 lb ai/gal	Ornamentals	1,000 gallons	NA	NA	NA	8 / 80	NA	NA
			0.01 lb ai/gal						8 / 80		
Mixing/Loading/Applying Using a Backpack Sprayer (13)	NA	NA	0.002 lb ai/gal	Turf & Ornamentals	40 gallons	NA	NA	NA	8 / 80	NA	NA
			0.01 lb ai/gal						8 / 80		
			5.5 lb ai/A	Turf	5 acres	NA	NA	NA	8 / 80	NA	NA
Loading/Applying Granulars Using a Belly Grinder (14)	NA	NA	0.68 lb ai/A	Turf	5 acres	NA	NA	NA	8 / 80	NA	NA
			1.4 lb ai/A						8 / 80		
			4.1 lb ai/A						8 / 80		

Table 10. Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Iprodione with Engineering Controls (Continued)

Exposure Scenario (Scen. #)	Eng. Cont. Dermal Unit Exposure[a] (mg/lb ai)	Eng. Cont. Inhalation Unit Exposure[b] (μg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	Eng. Con. Daily Dermal Exposure[f] (mg/day)	Eng. Con. Daily Inhalation Exposure[g] (mg/day)	Eng. Cont. Total Daily Dose (mg/kg/day)[h]	Number of Exposures per Year[i]	Eng. Cont. LADD[j] (mg/kg/day)	Eng. Cont. Total Cancer Risk[k]
Loading/Applying Using a Push-Type Granular Spreader (15)	NA	NA	0.68 lb ai/A 1.4 lb ai/A 4.1 lb ai/A	Turf	5 acres	NA	NA	NA	8 / 80 8 / 80 8 / 80	NA	NA
Mixing/Loading/Applying as a Seed Soak Treatment (16)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Mixing/Loading/Applying as a Commercial Seed Treatment in Slurry Form (17)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Mixing/Loading/Applying Solution as a Dip Treatment (18)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Flagger Risk											
Flagging Spray Applications (19)	0.00022	0.007	0.5 lb ai/A 1 lb ai/A	Ag	350 acres	0.039 0.077	0.0012 0.0025	4.5 E-5 9.0 E-5	10 / 100 4 / 40	6.2E-7 / 6.2E-6 4.9E-7 / 4.9E-6	2.7E-8 / 2.7E-7 2.2E-8 / 2.2E-7

Footnotes:

a Engineering Control Unit Exposure values represent : 1a,1b,1c,1d, 3a, 3b, closed mixing and loading; 2a, 2b, 2c water soluble bags; 4,5,6,7,10, 19 enclosed cab or cockpit

b Engineering Control Inhalation Unit Exposure reflects values taken from PHED V1.1 surrogate exposure tables (May 1997).

c Application rates come from values found in the LUIS report and on Iprodione labels. See Table 7 for particular examples.

d Crop Type or Target provides a general description of the intended uses of various products containing Iprodione. Separate categories are presented because of the distinct differences in application rates and acres treated.
Ag = agricultural crops and *Turf* = turfgrass including sod-farms, institutional areas and golf courses. *Ornamentals* = includes greenhouse, field, landscape, and conifer nurseries.

e Amount Handled Per Day values are from the EPA estimates of acreage treated, or volume handled in a single day for each exposure scenario of concern based on the application method.

f Eng. Con. Daily Dermal Exposure (mg/day) =Eng. Con. Unit Exposure (mg/lb ai) * Application Rate (lb ai/A or lb ai/gallon) * Amount Handled Per Day (acres/day or gallons/day).

g Eng. Con. Daily Inhalation Exposure (mg/day) = Eng. Con. Unit Exposure (μg/lb ai) * (1 mg/1000 μg) Conversion * Application Rate (lb ai/A or lb ai/gallon) * Amount Handled Per Day (acres/day or gallons/day).

h Eng. Con. Total Daily Dose = [Eng. Con Daily Dermal Exposure (mg/day) * 0.05 (Dermal Absorption Factor)'+ Eng. Con Daily Inhalation Exposure (mg/day)]/Body Weight (70 kg).

i Number of Exposures Per Year is based on maximum number of applications which represent private use. A factor of 10 was used to estimate commercial use.

j LADD (mg/kg/day) = Eng. Con. Total Daily Dose (mg/kg/day) * (Number of days exposure per year /365 days per year) * 35 years worked/70 year lifetime.

k Total Cancer Risk = LADD (mg/kg/day) * (Q_1*), where Q_1* = 4.39E-2 (mg/kg/day).

NA = Not Applicable. For scenarios 9 and 11 - 15 engineering controls are not available.

vi. Summary of Risk Concerns for Handlers, Data Gaps, and Confidence in Risk Estimates

Handler Scenarios with Risk Concerns. The calculations of short-term and intermediate-term inhalation risk indicate that inhalation MOEs are more than 100 at **baseline** for the all the assessed exposure scenarios **except** the following:

- (2a) mixing/loading wettable powder for aerial/chemigation application (at an application rate of 0.5 lb ai/acre, the short-term inhalation MOE was acceptable, but not at an application rate of 1.0 lb ai/acre).

The calculations of short-term and intermediate-term inhalation risks for scenario 2a indicates that with the **additional PPE,** inhalation MOEs are greater than 100.

As noted below in the data gaps discussion, several of the exposure scenarios could not be assessed due to lack of PHED surrogate data.

An engineering control assessment was carried out for enclosed cab aerial spray applications, and for wettable powders formulated in water soluble bags. The calculations of short-term and intermediate-term inhalation risks for these scenarios (Table 6) indicate that when engineering controls are employed (i.e., water soluble bags and enclosed cab), the MOEs are more than 100 for all assessed scenarios which include:

- (2a) mixing/loading wettable powder for aerial/chemigation application,
- (2b) mixing/loading wettable powder for groundboom application,
- (2c) mixing/loading wettable powder for orchard airblast application,
- (2d) mixing/loading wettable powder for professional application to turf with low pressure/high volume handgun,
- (5) applying sprays with a fixed-wing aircraft, and
- (6) applying sprays with a helicopter.

The calculations indicate that **cancer risks at baseline** are **greater than the 1.0E-4** for the following scenarios (refer to tables for specific scenarios-- for some scenarios the risks are below 1.0E-4 for private handlers or at lower application rates) :

- (1a) mixing/loading liquids for aerial/chemigation application,
- (1b) mixing/loading liquids for groundboom application (at application rates of 0.5 and greater than or equal to 1 lb ai/acre),
- (1c) mixing/loading liquids for orchard airblast sprayer application (commercial handlers only),
- (1d) mixing/loading liquids for professional application to turf grass using a low pressure/high volume handgun (to turf at an application rate of 5.5 lb ai/acre--commercial handlers only),
- (2a) mixing/loading wettable powder for aerial/chemigation application,

- (2b) mixing/loading wettable powder for groundboom application (commercial handlers only),
- (2c) mixing/loading wettable powder for orchard airblast sprayer application (commercial handlers only),
- (2d) mixing/loading wettable powder for professional application to turf with a low pressure/high volume handgun (commercial handlers only)
- (3a) mixing/loading dry flowables for chemigation application (commercial handlers only),
- (3b) mixing/loading dry flowables for groundboom application (to turf at an application rate of 5.5 lb ai/acre) (commercial handlers only),
- (11) mixing/loading/applying sprays using a low pressure hand wand (at an application rate of 0.01 lb ai/gallon for turf and ornamentals, and 5.5 lb ai/acre for turf) (commercial handlers only),
- (12) mixing/loading/applying sprays using a high pressure hand wand (at an application rate of 1 lb ai/acre for agriculture and 0.01 lb ai/gallon for ornamentals) (commercial handlers only),
- (14) mixing/loading/applying granulars using a belly grinder (commercial handlers only), and
- (15) mixing/loading/applying granulars with a push-type granular spreader at the 4.1 lb rate and higher (commercial handlers only).

The calculations indicate that **cancer risks at baseline** are **in the range of 1.0E-4 to 1.0E-6** for the following scenarios (refer to tables for specific scenarios-- for some scenarios the risks are greater than 1.0E-4 for commercial handlers or at higher application rates, and for others they are less than 1.0E-6 for private handlers or at lower application rates) :

- (1b) mixing/loading liquids for groundboom application,
- (1c) mixing/loading liquids for orchard airblast sprayer application (private handlers only),
- (1d) mixing/loading liquids for professional application to turf grass using a low pressure/high volume handgun,
- (2b) mixing/loading wettable powder for groundboom application,
- (2c) mixing/loading wettable powder for orchard airblast sprayer application,
- (2d) mixing/loading wettable powder for professional application to turf with a low pressure/high volume handgun (private handlers only),
- (3a) mixing/loading dry flowables for chemigation application,
- (3b) mixing/loading dry flowables for groundboom application,
- (4) loading granulars for tractor-drawn spreader applications,
- (7) applying sprays with a groundboom sprayer,
- (8) applying to orchards with an airblast sprayer,
- (10) applying granulars with a tractor-drawn spreader,
- (11) mixing/loading/applying sprays using a low pressure hand wand,
- (12) mixing/loading/applying sprays using a high pressure hand wand,
- (14) mixing/loading/applying granulars using a belly grinder,

- (15) mixing/loading/applying granulars with a push-type granular spreader, and
- (19) flagging spray applications.

The calculations indicate that **cancer risks at baseline** are **less than 1.0E-6** for the following scenarios:

- (4) loading granulars for tractor-drawn spreader applications (at the 0.68 rate for private handlers only),
- (7) applying sprays with a groundboom sprayer (all handlers at the 0.27 rate and less, and private handlers only at the 1.0 rate and less),
- (10) applying granulars with a tractor-drawn spreader (private handlers only at the 0.68 rate or less), and
- (15) mixing/loading/applying granulars with a push-type granular spreader (private handlers only at the 0.68 rate or less).

The calculations indicate that cancer risks **with additional PPE** are greater than 1.0E-4 for the following scenarios (refer to tables for specific scenarios-- for some scenarios the risks are below 1.0E-4 for private handlers or at lower application rates) :

- (1a) mixing/loading liquids for aerial/chemigation application,
- (2a) mixing/loading wettable powder for aerial/chemigation application,
- (3a) mixing/loading dry flowables for chemigation application, and
- (13) mixing/loading/applying sprays using a backpack sprayer (at an application rate of 5.5 lb ai/acre to turf).

The calculations indicate that **cancer risks with additional PPE** are **in the range of 1.0E-4 to 1.0E-6** for the following scenarios (refer to tables for specific scenarios-- for some scenarios the risks are greater than 1.0E-4 for commercial handlers or at higher application rates, and for others they are less than 1.0E-6 for private handlers or at lower application rates):

- (1a) mixing/loading liquids for aerial/chemigation application,
- (1b) mixing/loading liquids for groundboom application,
- (1c) mixing/loading liquids for orchard airblast sprayer application,
- (1d) mixing/loading liquids for professional application to turf grass using a low pressure/high volume handgun,
- (2a) mixing/loading wettable powders for aerial/chemigation application,
- (2b) mixing/loading wettable powder for groundboom application,
- (2c) mixing/loading wettable powder for orchard airblast sprayer application,
- (2d) mixing/loading wettable powder for professional application to turf with a low pressure/high volume handgun,
- (3a) mixing/loading dry flowables for chemigation application,
- (3b) mixing/loading dry flowables for groundboom application,
- (4) loading granulars for tractor-drawn spreader applications,
- (7) applying sprays with a groundboom sprayer,

- (8) applying to orchards with an airblast sprayer.
- (9) applying with a low pressure/high volume handgun to turfgrass.
- (10) applying granulars with a tractor-drawn spreader,
- (11) mixing/loading/applying sprays using a low pressure hand wand,
- (12) mixing/loading/applying sprays using a high pressure hand wand.
- (13) mixing/loading/applying using a backpack sprayer,
- (14) mixing/loading/applying granulars using a belly grinder
- (15) mixing/loading/applying granulars with a push-type granular spreader, and
- (19) flagging spray applications.

The calculations indicate that **cancer risks with additional PPE** are **less than 1.0E-6** for the following scenarios:

- (1b) mixing/loading liquids for groundboom application (at the 0.27 rate for all handlers, and for private handlers only at the 1.4 rate and less),
- (1c) mixing/loading liquids for orchard airblast sprayer application (at the 0.5 rate for all handlers and at the 1 lb rate and less for private handlers only),
- (1d) mixing/loading liquids for professional application to turf grass using a low pressure/high volume handgun (at the 1.4 rate for all handlers, and for private handlers only at the 5.5 rate),
- (2d) mixing/loading wettable powder for professional application to turf with a low pressure/high volume handgun (at the 1.4 rate for private handlers only),
- (4) loading granulars for tractor-drawn spreader applications (at the 1.4 rate and less for private handlers only),
- (7) applying sprays with a groundboom sprayer (all handlers at the 0.27 rate and less, and private handlers only at the 1.4 rate and less),
- (8) applying to orchards with an airblast sprayer (private handlers only at the 0.5 rate or less),
- (10) applying granulars with a tractor-drawn spreader (private handlers only at the 1.4 rate or less), and
- (11) mixing/loading/applying sprays using a low pressure hand wand (all handlers at rates of 0.01 lb ai/gallon or less),
- (13) mixing/loading/applying using a backpack sprayer (all handlers at the 0.002 lb ai/gallon rate or less, and private handlers only at rates of 0.01 lb ai/gallon or less),
- (15) mixing/loading/applying granulars with a push-type granular spreader (private handlers only at the 0.68 rate or less), and
- (19) flagging spray applications (private flaggers only).

The calculations indicate that cancer risks with **engineering controls** are **greater than 1.0E-4** for none of the exposure scenarios.

The calculations indicate that **cancer risks with Engineering Controls (closed mixing/loading, water soluble bags, enclosed cab or airplane cockpit)** are **in the range of 1.0E-4 to 1.0E-6** for

the following scenarios (refer to tables for specific scenarios-- for some scenarios the risks are less than 1.0E-6 for private handlers or at lower application rates) :

- (1a) mixing/loading liquids for aerial/chemigation application,
- (1b) mixing/loading liquids for groundboom application,
- (2a) mixing/loading wettable powders for aerial/chemigation application,
- (2b) mixing/loading wettable powder for groundboom application,
- (2c) mixing/loading wettable powder for orchard airblast sprayer application,
- (2d) mixing/loading wettable powder for professional application to turf with a low pressure/high volume handgun,
- (3a) mixing/loading dry flowables for chemigation application,
- (3b) mixing/loading dry flowables for groundboom application,
- (5) applying sprays with fixed wing aircraft,
- (6) applying sprays with a helicopter,
- (7) applying sprays with a groundboom sprayer,
- (8) applying to orchards with an airblast sprayer,
- (10) applying granulars with a tractor-drawn spreader,
- (19) flagging spray applications.

The calculations indicate that **cancer risks with Engineering Controls** are **less than 1.0E-6** for the following scenarios:

- (1b) mixing/loading liquids for groundboom application (all applications at the rate of 0.27 lbs ai/A only)
- (1c) mixing/loading liquids for orchard airblast sprayer application,
- (1d) mixing/loading liquids for professional application to turf grass using a low pressure/high volume handgun,
- (2b) mixing/loading wettable powder for groundboom application (private handlers only),
- (2c) mixing/loading wettable powder for orchard airblast sprayer application (all handlers at the 0.5 rate, and private handlers only at the 1.0 rate),
- (2d) mixing/loading wettable powder for professional application to turf with a low pressure/high volume handgun (all handlers at the rate of 1.4 lb ai/A and private handlers only at the rate of 5.5 lb ai/A),
- (3b) mixing/loading dry flowables for groundboom application (private handlers only at the 1.0 rate or less),
- (4) loading granulars for tractor-drawn spreader applications,
- (5) applying sprays with fixed wing aircraft (private applicators only),
- (6) applying sprays with a helicopter (private applicators only),
- (7) applying sprays with a groundboom sprayer (all applicators at the 0.27 rate, and private applicators only at all other rates),
- (8) applying to orchards with an airblast sprayer (all applicators at the 0.5 lb ai/A rate and private applicators only at the 1.0 rate),
- (10) applying granulars with a tractor-drawn spreader (private applicators only all rates),
- (19) flagging spray applications (flaggers supporting private applications only).

Data Gaps. Data gaps exist for the following scenarios:

- (9) - no chemical specific or PHED baseline dermal data exist for applying with a low pressure/high volume handgun to turfgrass.
- (16)- no chemical specific or PHED data exist for mixing/loading/applying as a seed soak treatment.
- (17) - no chemical specific or PHED data exist for mixing/loading/applying as a commercial seed treatment in slurry form.
- (18) - no chemical specific or PHED data exist for mixing/loading/applying solution as a dip treatment.

Data Quality and Confidence in Assessment. Several issues must be considered when interpreting the occupational exposure risk assessment. These include:

- No chemical specific data were provided; therefore, surrogate PHED data were used to assess exposure.

- Several handler assessments were completed using "low quality" PHED data due to the lack of a more acceptable data set (see Table 3 for the specific scenarios where only "low quality" data were available).

- Several generic protection factors were used to calculate handler exposures. These protection factors are general estimates and variability may be significant.

- Factors used to calculate daily exposures to handlers (including acres treated per day and gallons of liquid applied) are based on label directions and professional judgement for the broad range of sites, equipment, and methods that are possible for each scenario.

- Estimates of risk range from average or "typical" for private handlers, to high end for commercial handlers (i.e., it is possible but not likely that the actual risks to some commercial handlers could exceed those estimated here).

c. Occupational Post-Application Exposures and Risks

(I). Postapplication Exposure Scenarios

HED has determined that there are potential Postapplication exposures to individuals entering treated areas for the purpose of:

- Harvesting tree fruits and nuts, low-growing fruits, vegetables, and grapes;
- Pruning and propping fruit and nut trees;
- Harvesting and mowing of sod farm turf;
- Pruning, transplanting, and bundling flowers, ornamental shrubs, and vines; and
- Transplanting trees and other ornamentals.

The specific crop group/activity combinations likely to result in Postapplication exposures from Iprodione are listed below. These crop groups/activities were grouped based on assumed exposure level, preharvest interval (PHI), maximum number of applications per season and expected frequency of exposure. These crop groups/activities include the following:

- Grape harvesting, pruning, and staking: assumed to result in higher exposures than other activities such as propping or staking which would have a longer PHI and lower number of days of exposure;
- Stone fruit harvesting: assumed to result in higher exposures than other activities that have lower days of exposure;
- Almond harvesting: assumed to result in high exposure levels, but with lower PHI and lower application rates than stone fruit harvesting;
- Harvesting of small vegetables and fruits, including strawberries: assumed to result in higher exposures than activities such as scouting, thinning, or weeding , which have lower exposure frequencies;
- Harvesting dry bulb onions: assumed to have lower exposure frequencies than the harvesting of small fruits and vegetables group above;
- Non-harvesting activities such as weeding and scouting for crops such as beans, rice, lettuce, potatoes, and peanuts: assumed to have lower exposure levels and lower exposure frequencies than the harvesting scenarios;

- Ornamental shrub, vine and herbaceous plant harvesting, transplanting, pruning, and bundling of flowers: assumed to have high exposure levels and high exposure frequencies, and with greater application rates than fruits and vegetables;

- Sod farm harvesting and mowing: harvesting assumed to have high levels of exposure, but with low frequency; combined with low level more frequent exposures on days of mowing;

- Golf course mowing and maintenance: assumed to have low exposure levels, and high exposure frequency combined with high application rates and the potential for high number of applications per season; and

- Ginseng harvesting, scouting and weeding: assumed to be a discrete crop/activity set that would result in different exposures than those listed above.

One of these crop group/activities has been identified as a scenario yielding potential **chronic** exposure (i.e., ≥ 180 days of exposure/year) concern. These risks are summarized in Table 11. The potential chronic exposure reentry activities include:

- Mowing and maintenance of golf course turf: assumed to be a low exposure level (T_C = 500 cm^2/hour) activity;

All the crop groups and activities likely to result in Postapplication exposure from Iprodione have been assessed for **cancer risk**.

(ii). Data Sources and Assumptions for Scenarios Considered

No chemical-specific Postapplication human reentry or transferable residue data were submitted in support of the Reregistration of Iprodione. In lieu of these data, a surrogate Postapplication exposure assessment was conducted to determine potential risks for the previously mentioned representative scenarios.

Assumptions Used in Postapplication Exposure Calculations (Cancer and Non-Cancer Risks). The assumptions used in the calculations for occupational Postapplication risks include the following items, which are also summarized in Table 12:

- Application rates used for the calculations were derived using the following strategy:

  - -- Harvesting grapes = 0.75 lb ai/acre, which is the lower end of application rate range (0.75 and 1.0 lb ai/acre)
  - -- Harvesting almond trees = 0.5 lb ai/acre, which is the sole stated application rate of 0.5 lb ai/acre
  - -- Harvesting stone fruit trees = 0.75 lb ai/acre, which is the average of application rates (0.5 and 1.0 lb ai/acre)

Table 11. Occupational Postapplication Chronic Risks from Iprodione

Days After Treatment	Ornamentals[a]		
	DFR ($\mu g/cm^2$)[b]	Dermal Dose (mg/kg/day)[c]	MOE[d]
0	2.2	0.090	68
1	2.0	0.081	76
2	1.8	0.073	84
3	1.6	0.065	93
4	1.5	0.059	100

a This scenario represents the repotting, transplanting, harvesting and pruning of indoor and outdoor ornamentals.. Assumptions include a maximum application rate of 1.0 lb ai/acre, and a transfer coefficient (T_c) of 7,000 cm^2/hour, and hours exposed per day = 8 hours.

b DFR values derived from surrogate data.

c Dermal Dose (mg/kg/day) =([DFR ($\mu g/cm^2$]* transfer coefficient (T_c) * hours worked per day at the stated activity * 0.001 mg/μg * 0.05 dermal absorption rate/70 kg body weight.

d MOE = NOEL (mg/kg/day)/Dermal Dose (mg/kg/day), where NOEL = 6.1 mg/kg/day.

Table 12. Occupational Postapplication Scenarios and Cancer Risks from Iprodione

Exposure Activity/Crop or Target	Application Rate (lb ai/acre)	Transfer Coefficient (cm^2/hr)	Exposure Days per Year	Hours Worked per Day	Maximum Number of Applications per Season	Application Interval (days)	PHI[a] (days)	Assumed Avg. Entry Day[b]	DFR ($\mu g/cm^2$)[c]	LADD (mg/kg/day)[d]	Cancer Risk[e]
Grapes[f] (Harvesting/Pruning/Staking)	0.75	10,000	110	8	4	7	7	7	0.80	6.9E-3	3.0E-4
Almond Trees[g] (Harvesting)	0.5	10,000	60	8	4	7-14	NS (assume zero)	5	0.66	3.1E-3	1.4E-4
Stone Fruit Trees[h] (Harvesting)	0.75	10,000	60	8	4	7-14	7	9	0.65	3.1E-3	1.4E-4
Small Vegetables and Fruits, inc. Strawberries[i] (Harvesting)	0.75	3,500	120	8	2-10	7-14	0	5	0.99	2.4E-3	1.3E-4
Dry Bulb Onions[j] (Harvesting)	0.5	3,500	30	8	5-10	7-14	7	9	0.43	3.6E-4	1.6E-5
"Non-Harvest Activities in Vegetables, including beans, rice, lettuce, potatoes, peanuts[k] (e.g., weeding, scouting)	0.75	1,000	25	8	2-4	7-14	NA	5	0.99	1.9E-4	8.3E-6
Ornamentals[l] (Harvesting/Transplanting/ Pruning/Bundling Flowers)	3	7,000	90	8	NA	as required (assume 14 days)	NA	7	3.2	3.2E-2	1.4E-3
Sod Farms[m] (Harvesting/Mowing)	4.1	1,000	50	8	NA	14	NA	7	4.4	1.7E-3	7.5E-5
Golf Course Turf[n] (Mowing/Maintenance)	3	500	~~180~~	4	NA	14	NA	7	3.2	5.7E-4	2.5E-5
Ginseng[o] (Harvesting/Scouting/Weeding)	0.75	7,000	10	1	10	7-14	36	18	0.25	1.7E-5	7.5E-7

Table 12. *Occupational Postapplication Scenarios and Cancer Risks from Iprodione (Continued)*

Footnotes:

NA = Not applicable
NS = *Not specified*

a PHI values come from Iprodione labels.
b Assumed average entry day = (midpoint of the application interval - PHI) / 2 + PHI. For activities other than harvesting disregard PHI in the equation.
Example: For harvesting stone fruit trees, the midpoint of the application interval is (14 days +7 days/2) or 10.5 days. The assumed average entry day is therefore](10.5 days - 7 days)/2] + 7 days = 8.75 days, rounded to day 9.
c Surrogate DFR values derived from Residential SOPs. Surrogate DFR ($\mu g/cm^2$) = Application rate (lb ai/acre) x Conversion factor ($\mu g/cm^2$/lb ai/acre) x fraction of active ingredient retained on foliage. Fraction = 0.2 for day zero, and dissipates 10% daily thereafter.
d LADD = [DFR ($\mu g/cm^2$) x Tc (cm^2/hr) x mg/1,000 μg x hours exposed/day x exposure days/year x years of exposure x dermal absorption factor] / [body weight in kg x lifetime x 365 days/yr], where adult body weight = 70 kg, dermal absorption factor is 5%, lifetime = 70 years, and years of exposure is assumed to be 35 years.
e Cancer Risk = LADD (mg/kg/day) x Q1* (mg/kg/day), where Q1* = 4.39E-2.
f Application rate = lower end of range (0.75 and 1.0 lb ai/acre).
g Application rate = stated rate of 0.5 lb ai/acre. Days of exposure = 12 weeks x 5 days/week. PHI was not specified on label, and assumed to be zero days. Application interval on Iprodione labels not specified in days. Label guideline suggests first application pink bud, 2nd at full bloom, 3rd at petal fall and 4th application at up to 5 weeks after petal fall. For purposes of this assessment, application interval was assumed to be every 7-14 days.
h Application rate = average of 0.5 and 1.0 lb ai/acre rates.
I Application rate = average of rates (0.5 and 1.0 lb ai/acre). Days of exposure = 5-6 days/week, and 6-8 months per year.
j Application rate = lower end of range (0.5 and 0.75 lb ai/acre).
k Application rate = average of rates (0.5, 0.75 and 1.0 lb ai/acre). Days of exposure = once/week x 6 months. The risk calculations are based on an average application interval of 7-14 days. Two crops in this grouping have unique intervals:

- Risks to weeders and scouters of bean fields may be slightly underestimated because workers may be entering the fields closer to the time of application (i.e., 5 to 7 day application intervals), but this is expected to be offset by the low number of applications per season (i.e., 2).
- Risks to peanut farm workers may be slightly overestimated because the application interval for peanuts is 21 days and workers are expected to be entering fields later than the average reentry interval used for this calculation.

l Application rate = average of rates (2 and 4 lb ai/acre). Days of exposure = 5-6 days/week, 6-8 months/year period of pest pressure.
m Application rate = average of rates (2.7 and 5.5 lb ai/acre). Days of exposure = 50 weeks x 1 day/week. Transfer coefficient = weighted average of high exposure activity (harvesting) and low exposure activity (mowing).
n Application rate = lower end of range (2.7 and 5.5 lb ai/acre).
o Application rate = average of rates (0.5 and 1.0 lb ai/acre).

- -- Harvesting small fruits and vegetables, including strawberries = 0.75 lb ai/acre which is the average of application rates (0.5 and 1.0 lb ai/acre)
- -- Harvesting dry bulb onions = 0.5 lb ai/acre which is the lower end of application rate range (0.5 and 0.75 lb ai/acre)
- -- Weeding and scouting non-harvest vegetables, including beans, rice, potatoes, lettuce and peanuts = 0.75 lb ai/acre which is the average of application rates (0.5, 0.75, and 1.0 lb ai/acre)
- -- Transplanting, pruning, bundling of ornamental and flowers = 3.0 lb ai/acre which is representative of the application rate range (1.4 and 4.0 lb ai/acre)
- -- Harvesting and mowing sod farm turf = 4.1 lb ai/acre which is the average of application rates (2.7 and 5.5 lb ai/acre)
- -- Mowing and maintenance of golf course turf = 3.0 lb ai/acre which is the lower end of the range of application rates (2.7 and 5.5 lb ai/acre) (expected to have frequent prescriptive treatments rather than occasional corrective treatments).
- -- Harvesting, scouting, and weeding of ginseng = 0.75 lb ai/acre which is the average of application rates (0.5 and 1.0 lb ai/acre)

- Transfer coefficients (T_c) are assumed to be 10,000 cm^2/hr for high-contact harvesting (i.e., fruit and nut trees and grapes); 7,000 cm^2/hr for high contact activities in ornamental nurseries and greenhouses such as harvesting, transplanting, pruning and bundling of flowers; and a 7,000 cm^2/hr transfer coefficient was also assumed for harvesting, and scouting ginseng plants. Transfer coefficients are assumed to be 3,500 cm^2/hr for harvesting of low- growing fruit and vegetable crops (e.g., strawberries) and 1,000 cm^2/hr for activities such as weeding and scouting of low growing vegetables. A transfer coefficient of 1,000 cm^2/hr was estimated for harvesting and mowing of sod farms and is an average of the frequent but low T_c activities of mowing and infrequent but high T_c activity of harvesting. Golf course mowing and maintenance activities were assessed using a T_c of 500 cm^2/hr.

- Daily exposure is assumed to occur for 8 hours per day except for mowing and maintenance of golf course turf, and harvesting and scouting of ginseng. It is assumed that golf course workers will tend fairways and greens only half of their work day.

- Postapplication exposures to scouts and harvesters of ginseng farms are expected to be of high intensity, but for short periods of time (e.g., 1 hour per day for 10 days of the year).

- The average body weight of 70 kg is used, representing a typical adult.

- Exposure frequency is estimated to be 60 days/year for harvesting of fruit and nut trees (i.e., 12 5-day work weeks), 110 days/year for grapes, 120 days/year for small fruit and vegetable harvesting (including strawberries), 90 days/year for golf course mowing, 180 days/year for activities involving ornamentals, 50 days for sod farm maintenance, 30 days for harvesting of

dry bulb onions, 25 days for non-harvesting activities such as weeding and scouting low growing vegetables, etc., and 10 days/year for ginseng harvesting and scouting.

- Exposure duration is assumed to be 35 years. This represents a typical working lifetime.
- Lifetime is assumed to be 70 years.
- Dermal absorption is assumed to be 5 percent, as in the handler assessment[1].
- The Q1* used in the cancer assessment is 4.39×10^{-2} mg/kg/day.
- The cancer risks were assessed by estimating the day following an application that would represent the arithmetic mean of the total number of days of likely post-application entry by a worker between applications. For example, if the number of days between applications is 14 and the worker is expected to enter the treated area daily between applications, the estimated arithmetic-mean day would be day 7. The worker would be exposed to post-application residues from day 0 to day 14. Therefore, day 7 represents the mean or average day of entry. To calculate the arithmetic-mean post-application entry day for each post-application scenario, two variables are considered.

  (1)The retreatment interval -- i.e., the number of days between applications. When the retreatment interval is a range, the average of retreatment days is used. For example, if the retreatment interval ranges from 7 to 14 days, day 10.5 (7+14) ÷ 2) is used in the estimate.

  (2) The PHI - if the preharvest interval or PHI (i.e., the minimum number of days between the last application and harvest) is less than 14 days: the post-application activity likely to result in significant exposure is assumed to be harvesting. The PHI represents the earliest possible day of post-application entry by a worker to perform harvesting tasks. If the PHI is 14 days or greater, it is not used in the estimate, since the likely post-application activity is assumed to be a non-harvesting activity, such as scouting, weeding, pruning, or propping.

  2 examples of calculation of mean post application entry day follow:

  Stone fruit harvesting: where the retreatment interval is 7 to 14 days and the preharvest interval is 7 days.
  Average retreatment day is (7+14) ÷ 2 = day 10.5
  Number of possible entry days between applications is average retreatment day (day 10.5) minus the first possible day of entry (PHI day 7) = 3.5 days
  Mean of possible entry days between applications is 3.5 days ÷ 2 = day 1.75 of entry.

Possible entry-days range from first possible day of entry (day 7) to average retreatment day (day 10.5). Estimated mean post-application entry day is first possible entry day (PHI 7) + arithmetic mean of possible entry days (day 1.75) = Day 8.75 (rounded to day 9).

Non-harvesting, such as weeding and scouting, of small fruits and vegetables (including beans): the retreatment interval is 7 to 14 days and the preharvest interval is day 14.
Average retreatment day is (7+14) ÷ 2 = day 10.5.

Since the PHI is 14 days, the PHI is not included in the calculations (and a lower transfer coefficient appropriate for non-harvest activities is used). Therefore, the mean post-application entry day is the first possible entry day (day 0) + average retreatment day (day 10.5) ÷ 2 = day 5.25 (rounded to day 5).

(iii). Postapplication Exposure and Non-cancer Risk Estimates

The chronic Postapplication risks from Iprodione have been assessed using surrogate regression data. The DFR is derived from the application rate assuming an estimated 20 percent of the rate applied as initial dislodgeable residues, and an estimated 10 percent dissipation rate per day[6]. The equations used for the calculations in Table 11 are presented below.

Dislodgeable foliar residues (DFRs) were calculated as follows:

$$DFR\left(\frac{\mu g}{cm^2}\right) = AR\left(\frac{lb\ ai}{A}\right) \times CF\left(\frac{\mu g/cm^2}{lb\ ai/A}\right) \times F \times (1 - DR)^t$$

Where:

AR	=	average application rates which are highlighted in Table 12
CF	=	conversion factor is 11.2 lb per cm^2/lb ai per acre
F	=	fraction retained on foliage (20 percent)T
DR	=	daily dissipation rate (10 percent per day)
t	=	days after treatment, and is an assumed average reentry day identified in Table 12.

Daily Absorbed Doses were calculated as follows:

$$Dose\ (mg/kg/d) = \frac{(DFR\ (\mu g/cm^2) \times Tc\ (cm^2/hr) \times CF\left(\frac{1\ mg}{1{,}000\ \mu g}\right) \times Abs \times ED\ (hrs/day))}{BW}$$

Where:

DFR = daily DFR, as calculated above for the assumed average reentry day
Tc = transfer coefficient; 7,000 cm^2/hr for the transplanting, pruning, repotting, and bundling of ornamental shrubs, trees, vines and flowering and foliage plants
CF = conversion factor (i.e., 1 mg/1,000 μg)
Abs = dermal absorption (assume 5 percent)
ED = exposure duration; 8 hours worked per day for transplanting, pruning, bundling of ornamentals
BW = body weight (70 kg)

Chronic MOEs were calculated as follows:

$$\text{Chronic MOE} = \frac{\text{NOEL (mg/kg/day)}}{\text{Dose (mg/kg/day)}}$$

Where:

NOEL = 6.1 mg/kg/day1
Dose = calculated absorbed dermal dose

Table 11 presents the chronic dermal MOEs for the scenario identified with concern for potential chronic occupational exposure.

Postapplication Exposure and Risk Estimates for Cancer

Total cancer risk calculations were made using the formulas for DFR, LADD, and risk presented below. Certain assumptions, including transfer coefficient, application rate, and exposure duration, change with the different scenarios or activities. The assumptions used in the Iprodione DFR Postapplication risk calculations are described in the footnotes to Table 12, and are also summarized in the data assumptions section.

DFRs were calculated as follows:

$$DFR\left(\frac{\mu g}{cm^2}\right) = AR\left(\frac{lb\ ai}{A}\right) \times CF\left(\frac{\mu g/cm^2}{lb\ ai/A}\right) \times F \times (1 - DR)^t$$

Where:

AR = application rate. See Table 12, or Postapplication assumptions section for applicable rates for each Postapplication scenario

CF = conversion factor is 11.2 $\mu g/cm^2$ per lb/acre
F = fraction retained on foliage (20 percent)
DR = daily dissipation rate (10 percent per day)
t = days after treatment. See Table 12 or Postapplication assumptions section for the assumed average entry day (this is the day on which the cancer risk estimate is based for each individual scenario).

Lifetime Average Daily Dose (LADD) is calculated as follows:

$$LADD = \frac{DFR * Tc * ET * EF * ED * mg/1000\ \mu g * ABS}{BW * LT * 365\ d/yr}$$

Where:

DFR = dislodgeable foliar residue on day "t" ($\mu g/cm^2$)
T_c = transfer coefficient (cm^2/hr) (see Table 12 or Postapplication assumptions discussion)
ET = exposure time (hr/day) (see Table 12 or Postapplication assumptions discussion)
EF = exposure frequency (days/year) (see Table 12 or Postapplication assumptions discussion)
ED = exposure duration (35 years)
ABS = absorption factor (0.05);
BW = body weight (70 kg)
LT = lifetime (70 years).

Total cancer risks were calculated using the following formula:

$$RISK = LADD * Q1^*$$

where, $Q1^* = 4.39 \text{ X } 10^{-2}$ $(mg/kg/day)^{-1}$.

Summary of Postapplication Risk Concerns, Data Gaps, and Confidence in Estimates

Postapplication Scenarios with Risk Concerns. The results of the **chronic** dermal risk assessment indicate that an acceptable MOE (>100) is reached for the transplanting and pruning of ornamentals scenario on the 4th day after treatment.

The results of the **cancer** risk assessment indicate **risks greater than 1.0E-4** for the following crop type and activity groupings:

- Grape harvesting, pruning, staking, etc.,
- Almond harvesting,
- Stone fruit harvesting,

- Small fruit and vegetable harvesting, and
- Ornamental activities (harvesting, transplanting, pruning, bundling).

The results of the **cancer** risk assessment indicate **risks in the range of 1.0E-4 to 1.0E-6** for the following crop type and activity groupings:

- Dry bulb onion harvesting,
- Non-harvest activities in vegetables such as beans, rice, lettuce, potatoes, peanuts,
- Sod farm mowing and harvesting, and
- Golf course turf maintenance.

The results of the **cancer** risk assessment indicate **risks below 1.0E-6** for the following scenario:

- Ginseng post-application activities such as harvesting, scouting, weeding.

Harvesting small fruits and vegetables, including strawberries; and

Data Gaps, Quality, and Confidence

The following data gaps or uncertainties are associated with this assessment:

- No chemical-specific exposure or transferable residue data were submitted. As a result, all analyses were completed using surrogate data from sources such as PHED and assumptions related to the behavior and environmental fate of the chemical in the environment (e.g., dissipation of transferable residues).

- Factors used to calculate Postapplication risks (e.g., hours exposure per day or average reentry day) are based on labeling directions and best professional judgment due to lack of data specific to each crop/activity combination.

- The number of significant figures used to report cancer risks may indicate greater precision than the conservative default assumptions and data reliability can provide.

- Crop groupings for the Postapplication assessment are representative of general ranges of expected levels of exposure, and are based on application rate, PHI, exposure activity, and exposure duration. Risks may vary within these crops groupings.

- DFRs are estimated using the residential SOPs. The SOPs are designed to yield conservative estimates of residue levels. For Iprodione, however, these estimates may be less conservative because (1) environmental fate information indicates that Iprodione is likely to degrades more slowly than the 10% per day from the SOPs, and (2) potential additive effects of multiple applications have not been factored into the estimated DFRs.

- The "average reentry day" is derived from averages based on labeling instructions, and assumes regular retreatment and reentry. While this pattern may be typical for a growing season during which pest pressure is high, over a period of several years Iprodione treatments are not likely to be as regular or frequent as estimated in this assessment. The exception to would be for geographic regions and use sites where climatic (or other) conditions foster endemic pest pressure, and regular and frequent retreatment and reentry are necessary from year to year.

d. Residential and other Non-occupational Exposures and Risks

(I). Residential Handler Exposures and Risks

EPA has determined that residential and other non-occupational handlers are likely to be exposed during Iprodione use. The current labeling and anticipated use patterns indicate several major exposure scenarios based on the types of equipment that potentially can be used by homeowners to apply Iprodione. Those scenarios include: (1) mixing/loading/applying sprays with a low pressure handwand; (2) mixing/loading/applying using a backpack sprayer; (3) mixing/loading/applying using a garden hose-end sprayer; (4) loading/applying granulars using a belly grinder; (5) loading/applying granulars using a push-type lawn spreader; and (6) loading/applying granulars by hand as a spot treatment. Two other scenarios may also apply to homeowners, though no data are available for assessing potential exposures: (7) mixing/loading/applying as a seed soak treatment; and (8) mixing/loading/applying solution as a dip treatment.

(ii). Residential Handler Exposure Scenarios -Data and Assumptions

Residential handler exposure assessments were completed by EPA assuming a "baseline" exposure scenario (for homeowners, short sleeved shirt, short pants, shoes and sock, and no gloves or respirator). PHED values used to estimate daily unit exposure values were taken from the *Standard Operating Procedures (SOPs) for Residential Exposure Assessments* document dated December 1997. Table 13 summarizes the caveats and parameters specific to the surrogate data used for each scenario and corresponding exposure/risk assessment.

Table 13. Residential Exposure Scenario Descriptions for the Use of Iprodione

Exposure Scenario (Number)	Data Source	Standard Assumptions[a]	Comments[b]
Mixer/Loader/Applicator Descriptors			
Mixing/Loading/Applying Sprays with a Low Pressure Handwand (1)	SOPs for Residential Exposure Assessments (12/97)	5 gallons for small vegetable gardens, trees and ornamentals; and 20,000 ft^2 for turf	**Baseline**: Dermal and inhalation data = ABC grades, and hands data = All grade. Dermal = 9-80 replicates, hands 70 replicates; and inhalation = 80 replicates. Low confidence in hands, dermal data. Medium confidence in inhalation data. **PPE and Engineering Controls**: Not required for assessment.
Mixing/Loading/Applying Using a Backpack Sprayer (2)	SOPs for Residential Exposure Assessments (12/97)	5 gallons on fruit/nut trees, ornamentals, and small vegetable gardens; and 20,000 ft^2 for turf	**Baseline**: Dermal = AB grade; inhalation = A grade; and hands = C grade. Dermal = 9 to 11 replicates, hands 11 replicates; and inhalation = 11 replicates. Low confidence in dermal, and inhalation data. A 90% protection factor was used to back calculate "no glove" hand data from the gloved scenario. **PPE and Engineering Controls**: Not required for assessment.
Mixing/Loading/Applying Using a Garden Hose-end Sprayer (3)	SOPs for Residential Exposure Assessments (12/97)	50 gallons on trees, ornamentals and small vegetable gardens; and 20,000 ft^2 for turf	**Baseline**: Dermal and inhalation = C grade, and hands = E grade. Dermal, inhalation, and hands = 8 replicates each Low confidence in all data. **PPE and Engineering Controls**: Not required for assessment.
Mixing/Loading Granulars Using a Belly Grinder (4)	SOPs for Residential Exposure Assessments (12/97)	20,000 ft^2 and 1,000 ft^2 for turf	**Baseline:** Dermal and hands data = ABC grades, inhalation = AB grade. Dermal 20-45 replicates; hands = 23 replicates; and inhalation = 40 replicates. Medium confidence for hands, dermal and high confidence for inhalation **PPE and Engineering Controls**: Not required for assessment.
Loading/Applying Granulars Using a Push-type Lawn Spreader (5)	SOPs for Residential Exposure Assessments (12/97)	20,000 ft^2 and 1,000 ft^2 for turf	**Baseline:** Dermal and Hands data = C grade, and inhalation data = B grade. Hand = 15 replicates; dermal = 0-15 replicates; and inhalation = 15 replicates. Low confidence in hands, dermal data, and high confidence in inhalation data.. A 50% protection factor was used to "back calculate" a short sleeved shirt value from long sleeve shirt data **PPE and Engineering Controls**: Not required for assessment.
Loading/Applying Granulars by Hand as a Spot Treatment (6)	SOPs for Residential Exposure Assessments (12/97)	1,000 ft^2	**Baseline:** Dermal, hands and inhalation data = ABC grade. Hands, dermal and inhalation = 16 replicates. Medium confidence in all data. A 90% PF was applied to gloved hands data to back calculate "no glove" hand exposure **PPE and Engineering Controls**: Not required for assessment
Mixing/Loading/Applying as a Seed Soak Treatment (7)	NA	NA	**No Data**
Mixing/Loading/Applying Solution as a Dip Treatment (8)	NA	NA	**No Data**

Standard Assumptions based on HED estimates.
"Best Available" grades are defined by HED SOP for meeting Subdivision U Guidelines. Best available grades are assigned as follows: matrices with grades A and B data and a minimum of 15 replicates; if not available then grades A, B and C data and a minimum of 15 replicates; if not available, then all data regardless of the quality and number of replicates. Data confidence are assigned as follows: High= grades A and B and 15 or more replicates per body part; Medium= grades A, B, and C and 15 or more replicates per body part;
Low= grades A, B, C, D and E or any combination of grades with less than 15 replicates.

A = Not Applicable

The following assumptions and factors were used in the assessment:

- Maximum application rates for specific crops as recommended by the Iprodione labels were used to bracket risk levels associated with the various use patterns. No use data were provided concerning the application rates that are commonly used for Iprodione by homeowners. though survey data indicate that is common for homeowners to apply maximum (or higher) rates.

- Generally, the use of PPE and engineering controls are not considered feasible or appropriate for homeowners.

- For homeowner turf management, the following estimates of the square feet of a homeowners garden were used: 20,000 ft^2 for lawns areas, and 1,000 ft^2 for spot treatments.

- Estimates of spray application to small vegetable gardens and lawns include: 5 gallons per day for low pressure handwand and backpack sprayers, and 50 gallons per day for garden hose-end sprayers.

- PHED values represent a handler wearing short sleeve shirt, short pants, shoes and socks, and no gloves or respirator.

(iii). Residential Handler Exposure and Non-Cancer Risk Estimates

Calculations of homeowner handlers' exposure, dose, and risk were made using the formulas presented above for occupational handlers. Table 14 presents residential short and intermediate term inhalation risks associated with the handling of Iprodione.

Residential Handler Exposure and Risk Estimates for Cancer

Calculations of lifetime average daily dose (LADD) and cancer risk were performed using the formulas presented previously for the occupational handler cancer assessment.

Table 15 presents potential cancer risk estimates from dermal and inhalation exposures to Iprodione from residential handling activities.

Table 14. Residential Handler Exposures and Short-term and Intermediate-term Inhalation Risks for Iprodione (Baseline)

Exposure Scenario (Scen. #)	Baseline Inhalation Unit Exposure[a] (μg/lb ai)	Range of Application Rates[b] (lb ai/A)	Crop Type or Target[c]	Amount Handled per Day[d]	Baseline Inhalation Exposure[e] (mg/day)	Short-term Baseline Inhalation Dose[f] (mg/kg/day)	Int.-term Baseline Daily Inhalation Dose[g] (mg/kg/day)	Baseline Short-term MOE[h]	Baseline Int.-term MOE[i]
Mixer/Loader/Applicator Risks									
Mixing/Loading/Applying Sprays with a Low Pressure Handwand (1)	30	0.0026 lb ai/gal	Fruit/Nut Trees	5 gallons	0.00039	6.5E-6	5.6E-6	3,100,000	1,100,000
		0.01 lb ai/gal	Ornamentals	5 gallons	0.0015	2.5E-5	2.1E-5	800,000	290,000
		0.125 lb ai/1,000 ft²	Turf	20,000 ft²	0.075	1.3E-3	1.1E-3	15,000	5,500
		0.104 lb ai/gal	Vegetable/ Small Fruit Garden	5 gallons	0.016	2.7E-4	2.3E-4	74,000	27,000
Mixing/Loading/Applying Using a Backpack Sprayer (2)	30	0.0026 lb ai/gal	Fruit/Nut Trees	5 gallons	0.00039	6.5E-6	5.6E-6	3,100,000	1,100,000
		0.01 lb ai/gal	Ornamentals	5 gallons	0.0015	2.5E-5	2.1E-5	800,000	290,000
		0.125 lb ai/1,000 ft²	Turf	20,000 ft²	0.075	1.3E-3	1.1E-3	15,000	5,500
		0.104 lb ai/gal	Vegetable/ Small Fruit Garden	5 gallons	0.016	2.7E-4	2.3E-4	74,000	27,000
Mixing/Loading/Applying Using a Garden Hose-end Sprayer (3)	9.5	0.0026 lb ai/gal	Trees	50 gallons	0.0012	2.0E-5	1.7E-5	1,000,000	360,000
		0.01 lb ai/gal	Ornamentals	50 gallons	0.0048	8.0E-5	6.9E-5	250,000	88,000
		0.125 lb ai/1,000 ft²	Turf	20,000 ft²	0.024	4.0E-4	3.4E-4	50,000	18,000
		0.104 lb ai/gal	Vegetable/ Small Fruit Garden	50 gallons	0.049	8.2E-4	7.0E-4	24,000	8,700
Loading/Applying Granulars Using a Belly Grinder (4)	62	0.0941 lb ai/1,000 ft²	Turf	20,000 ft²	0.12	2.0E-3	1.7E-3	10,000	3,600
		0.0941 lb ai/1,000 ft²		1,000 ft²	0.0058	9.7E-5	8.3E-5	210,000	73,000

Table 14. Residential Short-term and Intermediate-term Inhalation Risks for Iprodione at Baseline (Continued)

Exposure Scenario (Scen. #)	Baseline Inhalation Unit Exposure[a] (µg/lb ai)	Range of Application Rates[b] (lb ai/A)	Crop Type or Target[c]	Amount Handled per Day[d]	Baseline Inhalation Exposure[e] (mg/day)	Short-term Baseline Inhalation Dose[f] (mg/kg/day)	Int.-term Baseline Daily Inhalation Dose[g] (mg/kg/day)	Baseline Short-term MOE[h]	Baseline Int.-term MOE[i]
Loading/Applying Granulars Using a Push-type Lawn Spreader (5)	6.3	0.0941 lb ai/1,000 ft²	Turf	* 20,000 ft²	0.012	2.0E-4	1.7E-4	100,000	36,000
		0.0941 lb ai/1,000 ft²		1,000 ft²	0.00059	9.8E-6	8.4E-6	2,000,000	730,000
Loading/Applying Granulars by Hand as a Spot Treatment (6)	470	0.0941 lb ai/1,000 ft²	Turf	1,000 ft²	0.044	7.3E-4	6.3E-4	27,000	9,700
Mixing/Loading/Applying as a Seed Soak Treatment (7)	No Data	No Data	Ag	No Data	No Data	No Data	No Data	No Data	No Data
Mixing/Loading/Applying Solution as a Dip Treatment (8)	No Data	No Data	Ag	No Data	No Data	No Data	No Data	No Data	No Data

Footnotes:

a Baseline Inhalation Unit Exposure values taken from PHED V1.1 reflect no respiratory protection.

b Application rates come from values found in the LUIS report and on Iprodione labels. For some scenarios, a range of application rates is used to represent different crops/sites based on application method.
Examples of application rates and source labels include:
0.0026 lb ai/gal applicable to stone fruit trees - EPA Reg. No. 264-562;
0.01 lb ai/gal ornamentals - EPA Reg. No. 264-563;
0.125 lb ai/1,000 ft turf - EPA Reg. No. 264-562; and
0.104 lb ai/gal potatoes and carrots - EPA Reg. No. 264-562.

c Crop Type or Target provides a general description of the intended uses of various products containing Iprodione. Separate categories are presented because of the distinct differences in application rates and acres or gallons treated or applied.

d Amount Handled Per Day values are from the EPA estimates of acreage treated, or volume handled in a single day for each exposure scenario of concern based on the application method.

e Baseline Inhalation Exposure (mg/day) = Unit Exposure (µg/lb ai) * (1 mg/1000 µg) Conversion * Application Rate (lb ai/ft² or lb ai/gal) * Amount Handled Per Day (ft²/day or gallons/day).

f Baseline Short-term Daily Inhalation Dose = Baseline Daily Inhalation Exposure (mg/day)/Body Weight (60 kg).

g Baseline Int.-term Daily Inhalation Dose = Baseline Daily Inhalation Exposure (mg/day)/Body Weight (70 kg).

h Baseline Short-term MOE = NOEL (20 mg/kg/day) / Short-term Baseline Daily Inhalation Dose (mg/kg/day).

i Baseline Intermediate-term MOE = NOEL (6.1 mg/kg/day) / Intermediate-term Baseline Daily Inhalation Dose (mg/kg/day).

ble 15. Residential Handlers' Combined Dermal and Inhalation Cancer Risk Assessment for Iprodione (Baseline)

Exposure Scenario (Scen. #)	Baseline Dermal Unit Exposure[a] (mg/lb ai)	Baseline Inhalation Unit Exposure[b] (μg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	Daily Dermal Exposure[f] (mg/day)	Daily Inhalation Exposure (mg/day)	Baseline Total Daily Dose[h] (mg/kg/day)	Number of Exposures per Year[i]	Baseline LADD[j] (mg/day)	Baseline Total Cancer Risk[k]
Mixer/Loader/Applicator Risk											
Mixing/Loading/Applying Sprays with a Low Pressure Handwand (1)	100	30	0.0026 lb ai/gal	Fruit/Nut Trees	5 gallons	1.3	0.00039	0.00093	4	5.1E-6	2.2E-7
			0.01 lb ai/gal	Ornamentals	5 gallons	5.0	0.0015	0.0036	4	2.0E-5	8.8E-7
			0.125 lb ai/ 1,000 ft²	Turf	20,000 ft²	250	0.075	0.18	2	5.2E-4	2.3E-5
			0.104 lb ai/gal	Vegetable/ Small Fruit Garden	5 gallons	52	0.016	0.037	4	2.0E-4	8.8E-6
Mixing/Loading/Applying Using a Backpack Sprayer (2)	5.1	30	0.0026 lb ai/gal	Fruit/Nut Trees	5 gallons	0.066	0.00039	0.000053	4	2.9E-7	1.3E-8
			0.01 lb ai/gal	Ornamentals	5 gallons	0.26	0.0015	0.00021	4	1.2E-6	5.3E-8
			0.125 lb ai/ 1,000 ft²	Turf	20,000 ft²	13	0.075	0.010	2	2.7E-5	1.2E-6
			0.104 lb ai/gal	Vegetable/ Small Fruit Garden	5 gallons	2.7	0.016	0.0021	4	1.2E-5	5.3E-7
Mixing/Loading/Applying Using a Garden Hose-end Sprayer (3)	30	9.5	0.0026 lb ai/gal	Trees	50 gallons	3.9	0.0012	0.0028	4	1.6E-5	7.0E-7
			0.01 lb ai/gal	Ornamentals	50 gallons	15	0.0048	0.011	4	6.0E-5	2.6E-6
			0.125 lb ai/ 1,000 ft²	Turf	20,000 ft²	75	0.024	0.054	2	1.5E-4	6.6E-6
			0.104 lb ai/gal	Vegetable/ Small Fruit Garden	50 gallons	160	0.049	0.11	4	6.0E-4	2.6E-5
Loading/Applying Granulars Using a Belly Grinder (4)	110	62	0.0941 lb ai/ 1,000 ft²	Turf	20,000 ft²	210	0.12	0.16	2	4.4E-4	1.9E-5
			0.0941 lb ai/ 1,000 ft²		1,000 ft²	10	0.0058	0.0073	2	2.0E-5	8.8E-7

Table 15. Residential Combined Dermal and Inhalation Cancer Risk Assessment for Iprodione at Baseline (Continued)

Exposure Scenario (Scen. #)	Baseline Dermal Unit Exposure[a] (mg/lb ai)	Baseline Inhalation Unit Exposure[b] (µg/lb ai)	Range of Application Rates[c] (lb ai/A)	Crop Type or Target[d]	Amount Handled per Day[e]	Daily Dermal Exposure[f] (mg/day)	Daily Inhalation Exposure[g] (mg/day)	Baseline Total Daily Dose[h] (mg/kg/day)	Number of Exposures per Year[i]	Baseline LADD[j] (mg/day)	Baseline Total Cancer Risk[k]
ading/Applying Granulars Using a sh-type Lawn Spreader (5)	3	6.3	0.0941 lb ai/ 1,000 ft²	Turf	20,000 ft²	5.6	0.012	0.0041	2	1.1E-5	4.8E-7
			0.0941 lb ai/ 1,000 ft²		1,000 ft²	0.28	0.00059	0.00021	2	5.8E-7	2.5E-8
ading/Applying Granulars by Hand a Spot Treatment (6)	430	470	0.0941 lb ai/ 1,000 ft²	Turf	1,000 ft²	40	0.044	0.029	2	7.9E-5	3.5E-6
ixing/Loading/Applying as a Seed ak Treatment (7)	No Data	No Data	No Data	Ag	No Data	No Data	No Data	No Data	No Data	No Data	No Data
lixing/Loading/Applying Solution a Dip Treatment (8)	No Data	No Data	No Data	Ag	No Data	No Data	No Data	No Data	No Data	No Data	No Data

a Baseline PHED V1.1 Dermal Unit Exposure values represent short pants, short sleeved shirt, no gloves, and open mixing/loading. (see *Exposure Scenario Descriptions Table* for further information).

b Baseline PHED V1.1 Inhalation Unit Exposure values reflect no respiratory protection.

c Application rates come from values found in the LUIS report and on Iprodione labels. For some scenarios, a range of application rates is used to represent different crops/sites based on application method. Examples of application rates and source labels include:
0.0026 lb ai/gal applicable to stone fruit trees - EPA Reg. No. 264-562;
0.01 lb ai/gal on ornamentals - EPA Reg. No. 264-563;
0.125 lb ai/1,000 ft² on turf - EPA Reg. No. 264-562; and
0.104 lb ai/gal on potatoes and carrots - EPA Reg. No. 264-562.

d Crop Type or Target provides a general description of the intended uses of various products containing Iprodione. Separate categories are presented because of the distinct differences in application rates and acres treated.

e Amount Handled Per Day values are from the EPA estimates of acreage treated, or volume handled in a single day for each exposure scenario of concern based on the application method.

f Daily Dermal Exposure (mg/day) = Unit Exposure (mg/lb ai) * Application Rate (lb ai/ft² or lb ai/gal) * Amount Handled Per Day (ft²/day or gallons/day).

g Daily Inhalation Exposure (mg/day) = Unit Exposure (µg/lb ai) * (1 mg/1000 µg) Conversion * Application Rate (lb ai/ft² or lb ai/gal) * Amount Handled Per Day (ft²/day or gallons/day).

h Baseline Total Daily Dose = [Baseline Daily Dermal Exposure (mg/day) * 0.05 (Dermal Absorption Factor) + Baseline Daily Inhalation Exposure (mg/day)]/Body Weight (70 kg).

I Number of Exposures Per Year is based on maximum number of applications which represent private use.

j Baseline LADD (mg/kg/day) = Baseline Total Daily Dose (mg/kg/day) * (Number of days exposure per year/365 days per year) * 35 years applied/70 year lifetime.

k Baseline Total Cancer Risk = Baseline LADD (mg/kg/day) * (Q_1*), where Q_1* = 4.39E-2 (mg/kg/day).

Summary of Risk Concerns for Homeowner-Handlers, Data Gaps, and Confidence in Exposure and Risk Estimates

Short and intermediate-term inhalation risks for homeowner-handlers were assessed as well as total cancer risks.

Homeowner Handler Risks. The calculations of short-term and intermediate-term inhalation risks indicate that inhalation MOEs are greater than 100 at baseline for all scenarios considered:

- (1) mixing/loading/applying sprays with a low pressure handwand;
- (2) mixing/loading/applying using a backpack sprayer;
- (3) mixing/loading/applying using a garden hose-end sprayer;
- (4) loading/applying granulars using a belly grinder; and
- (5) loading/applying granulars with a push-type lawn spreader; and
- (6) loading/applying granulars by hand as spot treatments.

The calculations of potential total cancer risk to homeowner handlers indicate that risks are greater than 1.0E-6 for the following scenarios:

- (1) mixing/loading/applying sprays with a low pressure handwand (turf and small fruits and vegetables only);
- (2) mixing/loading/applying using a backpack sprayer (turf only);
- (3) mixing/loading/applying using a garden hose-end sprayer (all sites except trees);
- (4) loading/applying granulars using a belly grinder for broadcast treatments; and
- (6) loading/applying granulars by hand as spot treatments.

The calculations of potential total cancer risk to homeowner handlers indicate that risks are below 1.0E-6 for all other scenarios.

Data Gaps. Data gaps exist for the following scenarios:

- (7) - no PHED data exist for mixing/loading/applying as a seed soak treatment.
- (8) - no PHED data exist for mixing/loading/applying solution as a dip treatment.

Data Quality and Confidence in Assessment. Several issues must be considered when interpreting the homeowner handler risk estimates:

- The PHED surrogate data for the garden hose-end sprayer scenario, application with a backpack sprayer scenario, application with a push type granular spreader scenario, and application with low pressure handwand scenario are low confidence due to low number of replicates and/or low quality data.

- The PHED values for loading/applying granulars by hand are based on gloved hand data; a 90% PF was used to estimate bare hand exposure for the baseline scenario.

- Factors used to calculate daily exposures to handlers (e.g., square footage treated per day or gallons of liquid applied) are based on labeling directions and professional judgement due to a lack specific usage data.

- The PHED values for low pressure handwand, backpack sprayer and garden hose-end sprayer are representative for treatment of low- to mid-level shrubs. The exposure data for these scenarios may underestimate exposures to head and upper body when homeowners make applications to trees.

(iv). Non-Occupational Postapplication Exposures and Risks

Once sprays and dusts have settled, Postapplication inhalation exposure is not expected to be significant. In addition, an appropriate dermal endpoint was not available for use in assessing non-cancer dermal risks. Consequently, only postapplication cancer risks have been assessed.

Postapplication Exposure Scenarios. EPA has determined that there are crop groups and activities likely to result in non-occupational Postapplication exposures from Iprodione. These crop groups/activities were grouped based on the assumed exposure level, PHI, maximum number of applications per season and expected frequency of exposure. These crop groups/activities include the following:

- Grape harvesting, pruning, and staking: assumed to result in higher exposures than other activities such as propping or staking which would have a longer PHI and lower number of days of exposure;
- Harvesting small vegetables and fruits, including strawberries: assumed to result in higher exposures than activities such as scouting, thinning, or weeding , which have longer PHIs and lower exposure frequencies;
- Ornamental shrub, vine and flowering or foliage plant transplanting, pruning, cutting, and bundling: assumed to have high exposure levels and high exposure frequencies, and with greater application rates than those applied to fruits and vegetables;
- Dermal exposure from residue on turf (adult and child);
- Incidental nondietary ingestion of residue on turf resulting from hand-to-mouth transfer (toddler);
- Ingestion of treated turfgrass (toddler); and
- Incidental ingestion of soil from treated areas (toddler).

Although youths, in addition to adults and toddlers, may also engage in Postapplication activities, they are expected to have lower transfer coefficients than adults (i.e., 5,000 cm^2/hour for harvesting fruit from trees as opposed to an adult value of 10,000 cm^2/hour)[6], and lower body weights (i.e., 39 kg as opposed to 70 kg for adults). The proportionally lower values for T_c and

body weight would result in similar exposure values for youths and adults. For this reason, a separate assessment for youths has not been performed. The exposure assessment for adults (LADD) would also apply to youths.

Although it is likely that toddlers would be exposed to Iprodione from dermal contact with, and incidental ingestion of grass, soil, or hand-to-mouth transfer, no risk assessment was performed for these scenarios because no relevant oral toxicological endpoints have been identified. The acute dietary endpoint of 20 mg/kg/day for Iprodione is applied only to females 13+. At present, HED has no toxicological data to elucidate the effects of Iprodione on toddlers. In addition, toddler cancer risks have not been quantified due to the fact that HED currently has no appropriate means to account for changing exposure parameters (i.e., activity duration, body weight, surface area, and transfer coefficient) as the toddler progresses through various age groups.

The crop groups and activities likely to result in residential Postapplication exposure from Iprodione have been assessed for **cancer risks** and are outlined in Table 16.

Data Sources for Scenarios Considered. No chemical-specific Postapplication human reentry or transferable residue data were submitted. In lieu of these data, a Postapplication exposure assessment was conducted using the Residential SOPs to determine potential risks for the representative scenarios.

Assumptions Used in Postapplication Exposure Calculations (Cancer Risks). Assumptions used in the calculations for residential Postapplication risks include the following:

- The cancer risks were assessed by estimating which day following an application would represent the arithmetic mean of the total number of days of likely post-application entry between applications. The same method employed for the worker scenarios has been used for non-occupational Postapplication assessment.

- A dermal absorption value of 5% was used in this assessment.

- The exposure duration for adults was assumed to be 35 years.

- Transfer coefficients were estimated to be 10,000 cm^2/hr for high-contact harvesting (i.e., grapes); 7,000 cm^2/hr for high contact activities involving ornamental shrubs, vines, flowering and foliage plants; and 3,500 cm^2/hr for harvesting small fruits and vegetables, including strawberries. The dermal transfer coefficient for turf exposure is estimated to be 43,000 cm^2/hr for adults.

- An average application rate of 3 lb ai/acre was used in the turfgrass and ornamental scenarios (range =1.4 lb ai/acre and 5.5 lb ai/acre). An average application rate of

ble 16. Residential Postapplication Scenarios and Cancer Risks from Iprodione

Exposure Activity/Crop or Target	Application Rate (lb ai/acre)	Contact Rate (cm^2/hr)[a]	Exposure Days per Year[b]	Years of Exposure	Hours Exposed per Day[a]	Maximum Number of Applications per Season[c]	Application Interval[c] (days)	PHI[c] (days)	Assumed Avg. Entry Day[d]	DFR[e] ($\mu g/cm^2$)	LADD[f] (mg/kg/day)	Cancer Risk[g]
rapes larvesting/Pruning/Staking)	0.75	10,000 cm^2/hr	8	35	0.67	4	7	0	4	1.1	5.8E-5	2.5E-6
mall Vegetables and Fruits, ıcluding Strawberries larvesting/Weeding/Staking)	0.75	3,500 cm^2/hr	24	35	0.67	2-10	7-14	0	5	0.99	5.5E-5	2.4E-6
ɪrnamentals Transplanting/Pruning / ıundling Flowers)	3	7,000 cm^2/hr	24	35	0.67	NS	7-14	NA	7	3.2	3.5E-4	1.6E-5
ıdults Dermal Contact with Turf)	3	43,000 cm^2/hr	78	35	2	2	NA	NA	45	0.059	3.8E-4	1.7E-5

A = Not applicable. NS = Not specified on Iprodione label.
Values come from *SOPs for Residential Exposure Assessments*[b]
Exposure days per year are based on Iprodione label directions and professional judgment. Turf exposure = 26 weeks x 3 days/wk.
Values derived from Iprodione labels for agricultural scenarios. Professional judgment employed in assumption of 2 turf applications per growing season..
Assumed average entry day = (average application interval - PHI) / 2 + PHI. For turf, applications are assumed to be made 2 times per year during a 180-day growing season, The average reentry period for the turfgrass scenarios is therefore average application interval of 90 days / 2, or 45 days.
DFR values derived from surrogate data. Surrogate DFR ($\mu g/cm^2$) = Application rate (lb ai/acre) x Conversion factor ($\mu g/cm^2$/lb ai/acre) x fraction of active ingredient retained on foliage. Fraction = 0.2 for day zero, and dissipates 10% daily thereafter.
For agricultural and dermal turf scenarios, LADD = [DFR ($\mu g/cm^2$) x Tc (cm^2/hr) x mg/1,000 μg x hours exposed/day x exposure days/year x years of exposure x dermal absorption factor] / [70 kg x 70 yr x 365 days/yr]
Cancer Risk = LADD (mg/kg/day) x Q1* (mg/kg/day), where Q1* = 4.39E-2.

0.75 lb ai/acre was used for the agricultural crop scenarios (i.e., harvesting of grapes and small fruits and vegetables), and was calculated from the application range of 0.5 to 1.0 lb ai/acre). The residential application rates used in the handler assessment were assessed in units of lb ai/gallon, due to application methods. These same rates were converted to lb ai/acre here, in order to calculate Postapplication risks.

- On the day of application, it was assumed that 20 percent of the application rate was available as dislodgeable turf residue, and dissipation takes place at a rate of 10% per day.
- Postapplication exposure for turf was assessed on the assumed average entry day (i.e., day 45 after application). This day was calculated assuming a 180-day season and a maximum of 2 applications per season.
- Adults were assumed to weigh 70 kg.
- The duration of exposure was assumed to be 0.67 hours per day, except for the turf scenario, which has an assumed duration of 2 hours per day.

(v). Postapplication Exposure and Non-Cancer Risk Estimates

No non-occupational crop groups or activities were identified as having potential chronic exposure.

(vi). Postapplication Exposure and Risk Estimates for Cancer

Non-occupational Postapplication scenarios were assessed for cancer risk; the results are summarized in Table 16. Total cancer risk calculations for the dermal scenarios were made using the formulas for DFR, LADD, and risk presented previously in the occupational Postapplication discussion.

As stated previously, toddler cancer risks have not been quantified due to the fact that HED currently has no appropriate means to account for the changing exposure parameters as the toddler progresses through the various age groups.

(vii). Summary of Postapplication Risks, Data Gaps, and Confidence

Non-occupational Postapplication scenarios with risk concerns. The results of the non-occupational Postapplication cancer risk assessment indicate that all residential Postapplication scenarios have risks greater than 1.0E-6.

Data gaps and uncertainties. The following data gaps or uncertainties were associated with this assessment:

- No chemical-specific exposure or transferable residue data were submitted. As a result, all analyses were completed using surrogate data from sources such as PHED and assumptions related to the behavior and environmental fate of the chemical in the environment (e.g., dissipation of transferable residues). Typically, these assumptions are considered to yield conservative estimates. However, because Iprodione degrades at a slow rate, the results of this assessment are expected to be somewhat less conservative than would be expected for other chemicals.

- Factors used to calculate Postapplication risks (e.g., hours exposure per day or average reentry day) are based on label directions and professional judgment due to an absence of specific usage data for each scenario. The estimates for frequency of retreatment and reentry into treated areas are expected to be typical for years in which pest pressure is high, but may represent the high end of exposure and risk over a period of several years including those in which pest pressure is not significant. Certain areas or sites may, however, experience high pest pressure on a yearly basis due to environmental or other factors.

- Crop groupings for the Postapplication assessment are assumed to be representative of general ranges of exposure, and are based on application rate, PHI, exposure activity and exposure duration. Risks are expected to vary within these crops groupings.

e. Incident Reports

The following data bases have been consulted for the poisoning incident data on the active ingredient Iprodione (PC Code: 109801):

OPP Incident Data System (IDS) - reports of incidents from various sources, including registrants, other federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992. Reports submitted to the Incident Data System represent anecdotal reports or allegations only, unless otherwise stated. Typically no conclusions can be drawn implicating the pesticide as a cause of any of the reported health effects. Nevertheless, sometimes with enough cases and/or enough documentation risk mitigation measures may be suggested.

Poison Control Centers - as the result of Data-Call-Ins issued in 1993, OPP received Poison Control Center data covering the years 1985 through 1992 for 28 organophosphate and carbamate chemicals. Most of the national Poison Control Centers (PCCs) participate in a national data collection system, the Toxic Exposure Surveillance System which obtains data from about 70 centers at hospitals and universities. PCCs provide telephone consultation for individuals and health care providers on suspected poisonings, involving drugs, household products, pesticides, etc.

California Department of Food and Agriculture (replaced by the Department of Pesticide Regulation in 1991) - California has collected uniform data on suspected pesticide poisonings since 1982. Physicians are required, by statute, to report to their local health officer all occurrences of illness suspected of being related to exposure to pesticides. The majority of the incidents involve workers. Information on exposure (worker activity), type of illness (systemic, eye, skin, eye/skin and respiratory), likelihood of a causal relationship, and number of days off work and in the hospital are provided.

National Pesticide Telecommunications Network (NPTN) - NPTN is a toll-free information service supported by OPP. A ranking of the top 200 active ingredients for which telephone calls were received during calendar years 1984-1991, inclusive has been prepared. The total number of calls was tabulated for the categories human incidents, animal incidents, calls for information, and others.

Incident Data System (IDS)

Please note that the following cases from the IDS do not have documentation confirming exposure or health effects unless otherwise noted.

A pesticide incident occurred in 1994, when a UPS driver was exposed to Iprodione after a bag spilled in his truck and he experienced dizziness. No further information on the disposition of the case was reported.

A pesticide incident occurred in 1995, when a male was sprayed with an aqueous use dilution mixture of Iprodione after the rupture of a gauge. He experienced numb lips and tongue, tingling fingers, and headache. No further information on the disposition of the case was reported.

A pesticide incident occurred in 1994, when a male was exposed to spray droplets on his face and neck after his garden was sprayed with Iprodione. Specific symptoms were not mentioned. No further information on the disposition of the case was reported.

A pesticide incident occurred in 1994, when individuals alleged they developed skin rashes while working in their garden three days after Iprodione and other pesticides were sprayed on crop fields. No further information on the disposition of the case was reported.

A pesticide incident occurred in 1996, when two workers prepared nonflowering ornamentals for shipment less than one day after foliar application of Iprodione and another pesticide. The products were applied at 1 lb and 3 lbs/100 gallons water. The workers wore rubber gloves to wrap loose vines around the main plants and developed a rash on their arms above the glove line the next day. No further information on the disposition of the case was reported.

California Data - 1982 through 1990

Detailed descriptions of 120 cases submitted to the California Pesticide Illness Surveillance Program (1982-1995) were reviewed. In 26 of these cases, Iprodione was used alone and was judged to be responsible for the health effects. Only cases with a definite, probable or possible relationship were reviewed. Iprodione ranked 84th as a cause of systemic poisoning in California. The table below presents the types of illnesses reported by year. None of the cases reported in the table below were reported to have been hospitalized. Table 20 gives the total number of workers that took time off work as a result of their illness.

Cases Due to Iprodione Exposure in California Reported by Type of Illness and Year, 1982-1995

Year	Illness Type					
	[b]Systemic	Eye	Skin	Respir.	[c]Comb.	Total
1982	-	-	-	-	-	-
1983	-	-	-	-	-	-
1984	-	-	2	-	-	2
1985	-	-	-	-	-	-
1986	1	1	-	-	-	2
1987	1	-	1	-	-	2
1988	-	-	-	-	-	-
1989	1	1	-	-	-	2
1990	-	1	4	-	-	5
1991	1	1	1	-	1	4
1992	-	-	-	-	-	-
1993	-	-	1	-	-	1
1994	4	1	2	-	-	7
1995	-	-	1	-	-	1
Total	8.00	5.00	12.00	0.00	1.00	26.00

[b] Category includes cases where skin, eye, or respiratory effects were also reported
[c] Category includes eye/skin illness

Number of Persons Disabled (taking time off work) or Hospitalized for Indicated Number of Days After Iprodione Exposure in California, 1982-1995.		
	Number of Persons Disabled	Number of Persons Hospitalized
One day	2	-
Two days	1	-
3-5 days	2	-
6-10 days	-	-
more than 10 days	-	-
unknown	-	-

A total of 12 persons had skin illnesses or 46% of 26 persons. Four of these cases occurred in 1990. A total of 8 persons had systemic illnesses or 31% of 26 persons. A variety of worker activities were associated with exposure to Iprodione as illustrated in the table below.

Illnesses by Activity Categories for Iprodione Exposure in California, 1982-1995						
Activity Category	Illness Category					
	[b]Systemic	Eye	Skin	Respiratory	[c]Combination	Total
Coincidental	-	-	1	-	-	1
Applicator	3	-	4	-	-	7
Resifield	3	1	6	-	-	10
Other	1	1	-	-	-	2
Mixloader	-	2	-	-	1	3
Driftexp	1	-	-	-	-	1
Clean/Fix	-	1	-	-	-	1
Pack/Proc	-	-	1	-	-	1
Total	8.00	5.00	12.00	0.00	1.00	26.00

[a] Mixloader = mixer and/or loader; Driftexp = exposure to pesticide that has drifted from intended targets; Clean/Fix = cleaning and/or repairing pesticide contaminated equipment; Pack/Proc = packing, processing, or retailing commodities
[b] Category includes cases where skin, eye, or respiratory effects were also reported
[c] Category includes eye/skin illness

According to the above activity categories, resifield (field worker exposed to residue in the field) that affected the skin were associated with the majority of the exposures. The skin illnesses occurred after Iprodione was applied to citrus and golf course greens and workers developed itchy rashes on hands, arms, face and legs. The resifield systemic illnesses included symptoms of headache and nausea. The ground applicator systemic illnesses included symptoms of weakness, eye irritation, muscle weakness to exposed side of face, and rashes on hands, neck, and face.

A pesticide incident occurred in 1996 that involved a male strawberry picker that was a harvester and did not have duties that involved handling any pesticides. Examination of the records for the fields in which he worked for 3 months prior to his illness showed potential exposure to 10 different pesticides, including Iprodione. He experienced flu-like symptoms and developed tonsillitis, coughing, and nosebleeds and was hospitalized for eight days and was diagnosed with pancytopenia. None of the other members of his crew, which had the same exposures, displayed these symptoms.

National Pesticide Telecommunication Network (NPTN)

On the list of the top 200 chemicals for which NPTN received calls from 1984-1991 inclusively, Iprodione was reported to be involved in sixteen human incidents.

Summary/Conclusions

Exposure to Iprodione can lead to skin illness requiring medical care. Skin rashes have been reported in field workers exposed to residues of Iprodione. A few cases (8) have reported relatively minor systemic symptoms such as headache, nausea, and dizziness. Three of the eight cases were reportedly due to field reentry. However, in none of the systemic cases was the exposure considered a probable or definite cause of the effects.

Recommendations

California data support the need for reentry intervals to prevent fieldworkers returning to fields immediately after application. Protective clothing to avoid skin rash is warranted for workers handling Iprodione (e.g., applicators and mixer/loaders).

4. Dietary Exposure and Risk Assessment/Characterization

a. Dietary Exposures from Food Sources

1. GLN 860.1200: Directions for Use

HED examined the registered food/feed use patterns and reevaluated the available residue chemistry database for adequacy in supporting these use patterns. A comprehensive summary of Iprodione food/feed use patterns, based on the product labels registered to Rhone-Poulenc is presented in Table 16. Label amendments are required to support continued uses of Iprodione on several crops. Details of the required label amendments are presented in the endnotes for GLN 860.1200 (Directions for Use) of appendix IV, Table D.

The Agency classifies the registered Section 24© uses of Iprodione on clover (seed crop; SLNs OR960011 and OR960012) and on peas (seed treatment; SLNs WA930026, WA930027) to be non-food uses because of adequate regulatory state controls and label use restrictions.

A tabular summary of the residue chemistry science assessments for Reregistration of Iprodione is presented in Table D. The status of Reregistration requirements for each guideline topic listed in Table D is based on the use patterns registered by the basic producer. When end-use product DCIs are developed (e.g., at issuance of the RED), RD should require that all end-use product labels (e.g., MAI labels, SLNs, and products subject to the generic data exemption) be amended such that they are consistent with the basic producer labels. A REFS search, conducted on December 11, 1996, identified six Iprodione end-use products (EPs) registered to Rhone-Poulenc Ag. Co. for use on a variety of food/feed crops. The EPs, registered under FIFRA Section 3, as well as the associated Special Local Need (SLN) products, registered under FIFRA Section 24(c), are listed in Appendix II, Table C.

2. GLN 860.1300: Nature of the Residue - Plants

The Reregistration requirements for plant metabolism are fulfilled. Acceptable studies depicting the qualitative nature of the residue in three dissimilar crops (peaches, peanuts, and rice) have been submitted and evaluated. Residues comprising the current Iprodione tolerance expression for plants accounted for 95% of the total radioactive residues (TRR) in peaches, 78% of the TRR in peanut hay, 75% of the TRR in rice head/stalks, and 60% of the TRR in rice straw. Other metabolites in each crop individually represented less than 10% TRR and/or less than 0.05 ppm. The residues to be regulated in plants should continue to be the parent, its isomer RP-30228, and metabolite RP-32490, which comprise the current tolerance expression for plants.

3. GLN 860.1300: Nature of the Residue - Animals

The Reregistration requirements for livestock metabolism are fulfilled provided label restrictions are in place. An additional ruminant metabolism study will not be required, provided that all applicable Iprodione end-use product labels prohibit use on cowpeas and prohibit the feeding of Iprodione-treated peanut hay to livestock animals, and that the 1x feeding level (theoretical maximum dietary intake) based on tolerances for feed items does not significantly increase above 30 ppm. If any registrant desires to support use on cowpeas or the feeding of peanut hay, or if new uses would significantly increase the 1x feeding level above 30 ppm, then a new ruminant metabolism study would be required to identify residues of concern and to generate samples for radiovalidation of an enforcement analytical method. An additional poultry metabolism study is not required.

The residues to be regulated in livestock should continue to be the parent, its isomer RP-30228, and metabolites RP-32490 and RP-36114 (see Figure 1) which comprise the current tolerance expression for livestock commodities.

4. GLN 860.1340: Residue Analytical Methods

Methods for determination of residues in/on plant commodities: The Pesticide Analytical Manual (PAM) Vol. II lists a GLC/ECD method, designated as Method I, for the determination of Iprodione residues of concern in/on plant commodities. Method I does not use benzene as a reagent and detects residues of Iprodione parent, Iprodione isomer RP-30228, and Iprodione metabolite RP-32490 as individual peaks on GLC. A successful Agency validation of Method I was carried out with kiwifruit.

The Chemistry Branch has determined that the proposed Common Moiety Method, wherein Iprodione tolerance residues are all hydrolyzed to dichloroaniline, is less suitable for enforcement than Method I of PAM Vol. II because of the potential for interference and a much longer time required for analysis. Other chemicals that can be converted to the dichloroaniline moiety will be assumed to interfere with detection of Iprodione residues, unless the registrant can provide data demonstrating otherwise. The Common Moiety Method, therefore, will not be forwarded to FDA for publication at this time.

The Common Moiety Method is, however, suitable for data collection provided it is modified to incorporate comments from Agency reviews and method validation. The Chemistry Branch notes that additional data are required for confined rotational crops, and the Iprodione residues of concern in/on rotational crops have not yet been determined. Because of the presence of conjugates not fully identified, the Common Moiety Method described may ultimately prove the most appropriate method available for determining Iprodione residues of concern in/on rotational crops.

The Iprodione Phase 4 Review waived the requirements for radiovalidation data for the analytical methods for plants since the parent and regulated metabolites are not likely to be bound or conjugated.

Methods for determination of residues in/on livestock commodities: There are presently no methods published in PAM Vol. II for the enforcement of Iprodione tolerances for livestock commodities. Morse Laboratories SOP Method-71 has been proposed as an enforcement method for the determination of non-hydroxylated Iprodione residues; this method converts non-hydroxylated Iprodione residues to dichloroaniline as a common moiety. For the purposes of Reregistration, Method-71 should be amended in accordance with the recommendations of the laboratory which conducted the independent laboratory validation. Because Method-71 uses benzene as a reagent, the registrant should justify the use of this substance, including an explanation of how substitution of a different solvent affects results.

The registrant should additionally provide independent laboratory validation data for the proposed method for determining hydroxylated Iprodione residues (e.g., RP-36114) in ruminant milk and tissues. Consistent with Iprodione Phase 4 Review, the registrant should explain why use of benzene and diazomethane as reagents is necessary.

Finally, the registrant should provide and/or develop confirmatory method(s) for the determination of major Iprodione residues (parent Iprodione and metabolites RP-32490 and RP-36114) in livestock commodities. This requirement is based on the fact that the proposed methods each involve conversion of Iprodione residues of concern to dichloroaniline; therefore, there is a concern for interference from other pesticides. If such confirmatory method(s) can be successfully developed and independently validated, then HED will submit them directly for Agency validation, rather than either of the common moiety methods currently proposed for livestock commodities.

5. GLN 860.1360: Multiresidue Methods

The registrant has submitted data on the determination of residues of Iprodione, Iprodione isomer RP-30228, Iprodione metabolite RP-32490, and Iprodione metabolite RP-36114 using FDA multiresidue methods. These data have been forwarded to FDA. Pending notification from FDA that further data are necessary, the Reregistration requirements for multiresidue method testing are satisfied for all Iprodione residues in current plant and livestock tolerance expressions.

The 1/94 FDA PESTDATA database (PAM Volume I, Appendix I) indicates that Iprodione and Iprodione metabolite isomer are completely recovered (>80%) by Multiresidue Methods Section 302 (Luke method; Protocol D), and that recovery is small (<50%) using Multiresidue Methods Section 303 (Mills, Onley, Gaither method; Protocol E, non-fatty foods). Iprodione is not recovered using Section 304 (Mills method; Protocol E, fatty foods).

6. GLN 860.1380: Storage Stability Data

The Reregistration requirements for storage stability data on plant commodity matrices are fulfilled. The data indicate that residues of Iprodione, its isomer RP-30228, and its metabolite RP-32490 are stable under frozen storage conditions for 24 to 34 months in/on representative raw

agricultural commodities of oilseeds, non-oily grains, leafy vegetables, root crops, and fruit and fruiting vegetables. No significant decline of residues was observed over the duration of study. These data validate the storage conditions and intervals of samples from the submitted field trials. The Reregistration requirements for storage stability data on livestock commodity matrices are also fulfilled. The data submitted provide guidance for storage parameters to be used with future studies. Future magnitude of residue studies should be supported by concurrent storage stability data.

7. GLN 860.1500: Crop Field Trials

Pending required label amendments for some crops, the Reregistration requirements for magnitude of the residue in/on the following raw agricultural commodities (RACs) are fulfilled: almonds (nutmeat and hulls); apricots; beans (dry and succulent); blueberries; boysenberries, broccoli; caneberries; carrots; cherries; currants; garlic; ginseng (dried root); grapes; kiwifruit; lettuce (head and leaf); mustard (Chinese); nectarines; onions (dry bulb); peaches; peanuts (nutmeat and hay); plums (fresh prunes); potatoes; raspberries; rice; strawberries. Overall, adequate field trial data depicting Iprodione tolerance residues following treatments according to the maximum registered use patterns have been submitted for the RACs listed above or have been translated where appropriate. Label revisions are required for some crops in order to reflect current Agency policies and/or to reflect the parameters of use patterns for which field trial data are available. Details of the required label amendments are presented in the endnotes for GLN 860.1200 (Directions for Use) of Table B. Refer to "Tolerance Reassessment Summary" section for recommendations with respect to established tolerance levels.

The temporary tolerances for tangelos and tangerines, and the time-limited tolerance for cottonseed have expired; therefore, they are not considered in this document.

8. GLN 860.1520: Processed Food/Feed

The Reregistration requirements for magnitude of the residue in the processed commodities of grapes, peanuts, plums, potatoes, and rice are fulfilled. Iprodione tolerance residues do not concentrate in the processed commodities of peanuts and potatoes. Iprodione tolerance residues concentrate during rice processing, and current tolerances for rice processed commodities are appropriate. Iprodione tolerance residues concentrate in raisins and prunes, and HED has recommended tolerance levels for these commodities. Refer to "Tolerance Reassessment Summary" section for recommendations with respect to established tolerance levels.

An acceptable cottonseed processing study was also submitted and evaluated in conjunction with the establishment of a time-limited tolerance for cottonseed. The previously requested bean processing data are no longer necessary since the Agency has determined that bean cannery residue is not a significant livestock feed item and has been removed from Table 1 (OPPTS GLN 860.1000).

9. GLN 860.1480: Meat, Milk, Poultry, and Eggs

The Reregistration requirements for magnitude of the residue in livestock are fulfilled. Acceptable ruminant and poultry feeding studies depicting the magnitude of Iprodione residues of concern have been submitted and evaluated. Ruminant feeding data are acceptable, up to a 10X feeding level of 200 ppm. A poultry feeding study was acceptable, up to a 10X feeding level of 100 ppm. Data from these feeding studies will be used to reassess the adequacy of the established tolerances for livestock commodities. As noted above, analytical method, livestock remains an outstanding data requirement. Depending on the development of an acceptable enforcement method to determine individual residues rather than common moieties, it may be necessary to adjust tolerance expressions and levels to reflect the residues detected by analytical enforcement method(s).

10. GLN 860.1400: Water, Fish, and Irrigated Crops

Phase 4 Review noted that label directions prohibit aquiculture in treated rice fields, and data on fish were not required. If this restriction is removed from the label, then fish studies would be necessary. Phase 4 Review also noted that data on residue decline in water were required for rice, and the registrant had made a commitment to conduct such a study. This requirement remains an outstanding data gap.

11. GLN 860.1460: Food Handling

Iprodione is presently not registered for use in food-handling establishments; therefore, no residue chemistry data are required under this guideline topic.

12. GLN 860.1850: Confined Accumulation in Rotational Crops

Additional data are required before Reregistration requirements for confined rotational crops can be considered fulfilled; data are required on the base hydrolysis of standards. The submitted field rotational study tentatively identified the parent Iprodione, its isomer (RP-30228), and metabolites RP-25040 and RP-44247 as the major radioactive residues in/on rotational crop commodities. The metabolites RP-25040 and RP-44247 are not included in the tolerance expression for primary crops. After resolution of this issue, study results will likely be presented to the HED Metabolism Committee. Depending on whether or not additional rotational crop metabolites need to be regulated, additional field rotational crop data (GLN 860.1900) may be required.

13. GLN 860.1900: Field Accumulation in Rotational Crops

As noted above, determination of the nature of the residue in confined rotational crops and a decision by the HED Metabolism Committee on the residues to be regulated in rotational crops

are necessary before the Agency can advise the registrant on the residue data required for extensive field trials.

Table 16. Food/Feed Use Patterns Subject to Reregistration for Iprodione (Case 2335).

Site Application Timing Application Type Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (ai)	Maximum Number of Applications Per Season	Maximum Seasonal Rate (ai)	Preharvest Interval (Days)	Use Limitations [1,2,3]
Almonds						
Foliar Ground/aerial	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FlC [264-482] 4 lb/gal SC/L [264-562] [4]	0.5 lb/A	4	2.0 lb/A	35 days after petal fall	Applications may be made in a minimum of 20 (ground) or 15 (aerial) gallons of water/A. Initial application should be made at pink bud stage and/or if conditions favorable for disease development persist. Three additional applications may be made at full bloom, petal fall, and up to 5 weeks after petal fall.
Apricots (See "Stone Fruits")						
Beans (Dry, Lima, and Snap)						
Foliar Ground/aerial	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FlC [264-482] 4 lb/gal SC/L [264-562]	1.0 lb/A	2	2.0 lb/A	14 (preforaging interval) or 45 (prefeeding interval for dry bean hay)	Applications may be made in a minimum of 40 (ground) or 10 (aerial) gallons of water/A. Initial application should be made at first bloom to when 10% of the plants have one open bloom. The second application may be made 5 to 7 days later or up to peak bloom. The feeding of snap or succulent bean hay to livestock is prohibited. Use on cowpeas is prohibited.
Blackberries (See "Caneberries")						
Blueberries (See "Bushberries")						

(continued: footnotes follow)

Table 16 (*continued*).

Site Application Timing Application Type Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (ai)	Maximum Number of Applications Per Season	Maximum Seasonal Rate (ai)	Preharvest Interval (Days)	Use Limitations [1,2,3]
Brassica (Cole) Leafy Vegetables (Seed Crop Only)						
Foliar Ground/aerial	50% WP [OR810055] [WA810052] [AZ880001] 4 lb/gal FIC [AZ880001] [OR960032] [WA960027]	2.0 lb/A	3 (Implied)	6.0 lb/A (Implied)	Not specified (NS)	Use limited to Brassica vegetables (broccoli, Brussels sprouts, cabbage, cauliflower, kale, kohlrabi, radish, rape, rutabaga, and turnips) grown for seed in AZ, CA, OR, and WA. In furrow treatment.
						Use limited to Brassica vegetables (broccoli, Brussels sprouts, cabbage, cauliflower, kale, kohlrabi, radish, rape, rutabaga, and turnips) grown for seed in AZ, CA, OR, and WA. Applications may be made in a minimum of 20 (ground) or 10 (aerial) gallons of water/A. Application should be made at full bloom, at pod set, and just prior to harvest. Use of treated crops, debris, or screenings for food or feed and the grazing of livestock on treated areas are prohibited.
	50% WP [CA850035]	1.0 lb/A	5	5.0 lb/A	NS	
Broccoli						
Foliar Ground	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FIC [264-482] 4 lb/gal SC/L [264-562]	1.0 lb/A	2	2.0 lb/A	0	Applications may be made in a minimum of 40 gallons of water/A. Initial application should be made after thinning (2- to 4-leaf stage) as a directed spray to the base of the plant and the adjacent soil surface. The second application may be made up to the day of harvest.

(continued; footnotes follow)

Table 16 (*continued*).

Site Application Timing Application Type Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (ai)	Maximum Number of Applications Per Season	Maximum Seasonal Rate (ai)	Preharvest Interval (Days)	Use Limitations [1,2]
Bushberries (Including Blueberries, Highbush and Lowbush; Currants; Elderberries; Gooseberries; and Huckleberries)						
Foliar Ground	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FIC [264-482]	1.0 lb/A	4	4.0 lb/A	0	Applications may be made in a minimum of 100 gallons of water/A. Initial application should be made at early bloom (5 to 10% bloom) and again at full bloom. Two additional applications may be made at 14-day intervals.
Caneberries (Including Blackberries, Loganberries, Red and Black Raspberries, and Cultivars and/or Hybrids)						
Foliar Ground	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FIC [264-482] 4 lb/gal SC/L [264-562]	1.0 lb/A	4	4.0 lb/A	0	Applications may be made in a minimum of 100 gallons of water/A. Initial application should be made at early bloom (5 to 10% bloom) and again at full bloom. Two additional applications may be made at 14-day intervals.
Carrots						
Foliar Ground/aerial	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FIC [264-482] 4 lb/gal SC/L [264-562]	1.0 lb/A or 0.5 lb/A (when tank mixed with other fungicides)	4 or 10 (tank mix rate)	4.0 lb/A or 5.0 lb/A (tank mix rate)	0	Applications may be made in a minimum of 10 gallons of water/A. Initial application should be made when conditions become favorable for disease development. Additional applications may be made at 7- to 14-day intervals.

(continued; footnotes follow)

Table 16 (*continued*).

Site Application Timing Application Type Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (ai)	Maximum Number of Applications Per Season	Maximum Seasonal Rate (ai)	Preharvest Interval (Days)	Use Limitations [1,2,3]
Carrots (continued)						
Seed soak treatment Ground	50% WP [WA940001] 4 lb/gal FlC [WA940006]	0.25 lb/6 gal	1	0.25/6 gal	1	Use limited to seed treatment of carrots in WA. Application should be made as a seed soak. Treat 3 lbs of carrots seeds per 6 gallons of soaking solution for 24 hours at 30 C. Allow the seeds to thoroughly dry before packaging or planting. Use of treated seed for food or feed purposes is prohibited.
Cherries (See "Stone Fruits")						
Chinese Mustard						
Foliar Ground	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FlC [264-482] 4 lb/gal SC/L [264-562]	0.5 lb/A	4	2.0 lb/A	10	Use limited to FL. Applications may be made in a minimum of 50 gallons of water/A. Initial application should be made when conditions become favorable for disease development. Additional applications may be made at 7- to 14-day intervals.
Clover (Seed Crop Only)						

(continued; footnotes follow)

Table 16 (*continued*).

Site Application Timing Application Type Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (ai)	Maximum Number of Applications Per Season	Maximum Seasonal Rate (ai)	Preharvest Interval (Days)	Use Limitations [1,2,3]
Foliar Ground	50% WP [OR960011] 4 lb/gal FIC [OR960012]	1.0 lb/A	2	2.0 lb/A	NS	Use limited to crimson clover grown for seed in OR. Applications may be made with surfactants and in a minimum of 12 gallons of water/A. Initial application should be made when disease first appears. A second application may be made prior to the 10-inch growth stage or no later than May 31. The product labels prohibit the following: use on crimson clover grown for livestock feed; feeding or grazing of livestock on treated crimson clover; cutting of treated crimson clover for forage and hay; and use of harvested seed for sprouting. No portion of the treated field including seed, seed screenings, hay, forage, or stubble may be used for human or animal feed.
Cotton						
In-furrow at planting Ground	50% DF [264-524] 50% WP [264-253] 4 lb/gal FIC [264-482]	0.02 lb/1,000 feet of row or 0.3 lb/A (with 30-inch row spacing)	NS	NS	--	Application may be made in a minimum of 2.5 gallons of water/A. The grazing or feeding of cotton forage to livestock is prohibited.
Currants (See "Bushberries")						
Elderberries (See "Bushberries")						

(continued; footnotes follow)

Table 16 (*continued*).

Site Application Timing Application Type Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (ai)	Maximum Number of Applications Per Season	Maximum Seasonal Rate (ai)	Preharvest Interval (Days)	Use Limitations [1,2,3]
Garlic						
In-furrow at planting Ground	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FlC [264-482]	2.0 lb/A	1	2.0 lb/A	--	Application may be made in a minimum of 20 gallons of water/A. Application should be made as an in-furrow spray in sufficient water to obtain thorough coverage of the open furrow and covering soil.
Ginseng						
Foliar Ground	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FlC [264-482]	1.0 lb/A or 0.75 lb/A (when tank mixed with other fungicides)	5	5.0 lb/A	36	Applications may be made in a minimum of 10 gallons of water/A. Initial application should be made when conditions become favorable for disease development. Additional applications may be made at 7- to 14-day intervals.
Gooseberries (See "Bushberries")						
Grapes						
Foliar Ground	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FlC [264-482] 4 lb/gal SC/L [264-562]	1.0 lb/A	4	4.0 lb/A	7	Applications may be made in a minimum of 50 gallons of water/A. Initial application should be made at early to mid bloom, the second prior to bunch closing, the third at beginning of fruit ripening, and the fourth prior to harvest.
Huckleberries (See "Bushberries")						
Lettuce (Head and Leaf)						

(continued; footnotes follow)

Table 16 (*continued*).

Site Application Timing Application Type Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (ai)	Maximum Number of Applications Per Season	Maximum Seasonal Rate (ai)	Preharvest Interval (Days)	Use Limitations [1,2,3]
Foliar Ground/aerial	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FlC [264-482] 4 lb/gal SC/L [264-562]	1.0 lb/A	3	3.0 lb/A	14	Applications may be made in a minimum of 40 gallons of water/A; aerial application can only be used for the first spray. Initial application should be made at the 3-leaf stage to just after thinning. Two additional applications may be made at 10-day intervals.
Loganberries (See "Caneberries")						
Nectarines (See "Stone Fruits")						
Onions (Dry Bulb)						
Foliar Ground/aerial	50% DF [264-524] 50% WP [264-453] [264-532] [CA860064] 4 lb/gal FlC [264-482] 4 lb/gal SC/L [264-562]	0.75 lb/A or 0.5 lb/A (when tank mixed with other fungicides)	5 or 10 (tank mix rate)	3.75 lb/A or 5.0 lb/A (tank mix rate)	7	Applications may be made in a minimum of 50 (ground), 10 (aerial), or 6 (aerial CA860064) gallons of water/A. Initial application should be made when conditions become favorable for disease development. Additional applications may be made at 7- to 14-day intervals.
Peaches (See "Stone Fruits")						

(continued; footnotes follow)

Table 16 (*continued*).

Site Application Timing Application Type Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (ai)	Maximum Number of Applications Per Season	Maximum Seasonal Rate (ai)	Preharvest Interval (Days)	Use Limitations [1,2,3]
Peanuts						
Foliar Ground	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FlC [264-482]	1.0 lb/A	3	3.0 lb/A	10	Applications may be made in a minimum of 40 gallons of water/A. Initial application should be made when conditions become favorable for disease development. Two additional applications may be made at 14- to 21-day intervals. The feeding of peanut hay to livestock is prohibited. Use of the 50% WP [EPA Reg. No. 264-532] is limited to states other than CA.
Peas (Seed Treatment)						
Seed treatment Ground	50% WP [WA930026] [WA930027]	2.8 oz/cwt	1	2.8 oz/cwt	--	Use limited to seed treatment of peas in WA. Application should be made in sufficient water to ensure complete seed coating. Seeds should be allowed to dry before packaging or planting. Use of treated seed for food or feed purposes is prohibited. Treated seed must be labeled: "For export to Sweden only - not to be sold or offered for sale in the U.S."
Plums (See "Stone Fruits")						

(continued; footnotes follow)

Table 16 (*continued*).

Site Application Timing Application Type Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (ai)	Maximum Number of Applications Per Season	Maximum Seasonal Rate (ai)	Preharvest Interval (Days)	Use Limitations [1,2,3]
Potatoes						
Foliar Ground/aerial	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FIC [264-482] 4 lb/gal SC/L [264-562]	1.0 lb/A	4	4.0 lb/A	14	Applications may be made in a minimum of 10 gallons of water/A; aerial equipment can only be used for the first application. Initial application should be made when conditions become favorable for disease development. Additional applications may be made at 7- to 28-day intervals.
	1.5 lb/gal SC/L [ID960011] [MO960002] [OR960033] [MN960004]	0.56 lb/A	7	4.0 lb/A		
Foliar Ground	50% WP [CA880019]	1.0 lb/A	2	2.0 lb/A		Use limited to CA. Applications may be made in a minimum of 10 gallons of water/A. Initial application should be made prior to row closing. A second application may be made 28 days later.
	50% WP [CA900013]	1.0 lb/A	4	4.0 lb/A	--	Use limited to greenhouse-grown potatoes in CA. Applications may be made in a minimum of 100 gallons of water/A. Initial application should be made when conditions favorable for disease development persist. Three additional applications can be made at 7- to 10-day intervals. Use of treated commodity for food/feed is prohibited.
Raspberries (See "Caneberries")						
Rice						

(continued; footnotes follow)

Table 16 (*continued*).

Site Application Timing Application Type Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (ai)	Maximum Number of Applications Per Season	Maximum Seasonal Rate (ai)	Preharvest Interval (Days)	Use Limitations [1,2,3]
Foliar broadcast Aerial	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FlC [264-482] [264-520]	0.5 lb/A	2	1.0 lb/A	No later than 75% heading stage	Applications may be made in a minimum of 10 gallons of water/A. Initial application should be made between joint movement and booting stages. A second application may be made 14 days after the first application, but no later than 75% heading. Use of 50% WP (EPA Reg. No. 264-532) and 4 lb/gal FlC (EPA Reg No. 264-520) is limited to states other than CA. Application to areas where catfish and crayfish are commercially cultivated is prohibited. Endangered species restrictions are specified for use in AR.
Stone Fruits (Including Apricots, Cherries, Nectarines, Peaches, Plums, and Prunes)						
Foliar Ground/aerial	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FlC [264-482] 4 lb/gal SC/L [264-562]	1.0 lb/A	4	4.0 lb/A	7	Applications may be made in a minimum of 20 (ground) or 15 (aerial) gallons of water/A. Initial application should be made at bud stage and/or if conditions favorable for disease development persist. Three additional applications can be made at 7- to 14-day intervals.

(continued; footnotes follow)

Table 16 (*continued*).

Site Application Timing Application Type Application Equipment	Formulation [EPA Reg. No.]	Maximum Single Application Rate (ai)	Maximum Number of Applications Per Season	Maximum Seasonal Rate (ai)	Preharvest Interval (Days)	Use Limitations [1,2,3]
Strawberries						
Preplant dip Ground	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FlC [264-482] 4 lb/gal SC/L [264-562]	1.0 lb/100 gal	1	1.0 lb/100 gal	--	Application may be made as a preplant dip (5 minutes) immediately prior to planting.
Foliar Ground/aerial	50% DF [264-524] 50% WP [264-453] [264-532] 4 lb/gal FlC [264-482] 4 lb/gal SC/L [264-562]	1.0 lb/A or 0.5 lb/A (when tank mixed with other fungicides)	4 or 10 (tank mix rate)	4.0 lb/A or 5.0 lb/A (tank mix rate)	0	Applications may be made in a minimum of 100 (ground) or 10 (aerial) gallons of water/A. Initial application should be made no later than 10% bloom. Additional applications can be made at 7- to 14-day intervals.

1 The restricted entry interval (REI) is 12 hours.

2 The following rotational crop restrictions are established: (i) beans, broccoli, carrots, Chinese mustard, cotton, garlic, lettuce, onions (dry bulb), peanuts, potatoes, and rice may be rotated after harvest; and (ii) cotton, root crops, and tomatoes may be rotated one month following the last Iprodione application.

3 Grazing restrictions are established for almonds, grapes, and stone fruits. The grazing of animals in treated orchards is prohibited. The feeding of cover crops grown in treated orchards is prohibited.

4 Use directions for the 4 lb/gal SC/L (EPA Reg. No. 264-562) are for homeowner use.

b. Tolerance Reassessment Summary

Tolerances for Iprodione are published in 40 CFR §180.399. Tolerances had been established in/on almonds, apricots, beans, blueberries, boysenberries, broccoli, caneberries, carrots, cherries, currants, garlic, ginseng, grapes, kiwi, lettuce, onions, nectarines, peaches, peanuts, plums, potatoes, raspberries, rice and strawberries. The available data support the established tolerances with the proposed reassessments: revoke raspberries; lower the tolerance on grapes from 60 ppm to 10 ppm, and on peaches from 20 ppm to 0.05 ppm; and raise the tolerance on prunes from 20 ppm to 80 ppm, poultry fat from 3.5 ppm to 7 ppm, poultry liver from 5 ppm to 7 ppm, and poultry meat by-products from 1 ppm to 7 ppm (Abbotts 1997).

Tolerances for residues of Iprodione in/on plant commodities [40 CFR §180.399 (a), (c), and (d)(1), and 40 CFR §180.31], processed food commodities [40 CFR §185.3750], and processed feed commodities [40 CFR §186.3750] are expressed in terms of the combined residues of Iprodione parent, its isomer, and one metabolite. Following evaluation of acceptable plant metabolism studies, HED has determined that the Iprodione residues of concern that warrant regulation in/on plant commodities should continue to be those that comprise the current tolerance expression for plants.

Tolerances for residues of Iprodione in livestock commodities [40 CFR §180.399 (b)] are expressed in terms of the combined residues of Iprodione parent, its isomer, and two metabolites, all expressed as Iprodione equivalents. Following evaluation of acceptable livestock metabolism studies, HED has determined that the Iprodione residues of concern that warrant regulation in livestock commodities should continue to be those that comprise the current tolerance expression for livestock.

The Agency has recently updated the list of raw agricultural and processed commodities and feedstuffs derived from crops (Table 1, OPPTS GLN 860.1000). As a result of changes to Table 1 (OPPTS GLN 860.1000), Iprodione tolerances for certain RACs which have been removed from the livestock feeds table need to be revoked. Some commodity definitions must also be corrected. A summary of Iprodione tolerance reassessments is presented in Table 17.

Tolerances Listed Under 40 CFR §180.399 (a)

Pending label amendments for some crops, adequate data are available to reassess the established tolerances for the following commodities, **as defined**: almonds, hulls; almonds, nutmeat; apricots; beans, dried, vine hay; beans, dry; beans, forage; beans, succulent; blueberries; boysenberries; broccoli; caneberries; carrots; cherries (sour); cherries (sweet) (pre- and postharvest); currants; garlic; ginseng; grapes; kiwi fruit (imported); lettuce; onions, dry bulb; nectarines (pre- and postharvest); peaches (pre- and postharvest); peanuts; peanut forage; peanut hay; peanut hulls; plums (pre- and postharvest); potatoes; raspberries; rice, grain; rice, straw; and strawberries.

Explanations and rationales for tolerance adjustments of certain RACs are presented below.

Bean forage and hay: Provided labels are amended such that Iprodione use on cowpeas is prohibited, no tolerances are required on the forage and hay of beans. Therefore, the established tolerances for "beans, dried, vine hay" and "beans, forage", each established at 90 ppm, should be revoked.

Blueberries and currants: The available field trial data for blueberries will be translated to currants.

Boysenberries and raspberries: The established tolerances of 15 ppm for boysenberries and raspberries should be revoked since Iprodione residues on these crops, as a result of registered uses, are covered by the established tolerance for caneberries.

Ginseng: The appropriate RAC for ginseng is dried root (Table 1, OPPTS GLN 860.1000). A Section 408 tolerance of 4 ppm for "ginseng, root, dried" should be established concomitant with the revocation of the tolerance of 2 ppm for "ginseng".

Grapes: Review of residue chemistry data determined that appropriate tolerance levels are 10 ppm for grapes and 15 ppm for the processed commodity raisins.

Peanut, hay: The registrant has submitted label amendments to prohibit the feeding of peanut hay to livestock in order to mitigate risk. HED previously recommended that the established tolerance for peanut hay should be revoked (Abbotts 1996). The established tolerances for peanut forage and hulls should be revoked since these items are not considered significant livestock feed items (Table 1, OPPTS GLN 860.1000).

Plums: An appropriate Section 408 tolerance is 80 ppm for prunes based on a concentration factor of 4x and the existing plum (fresh prune) tolerance of 20 ppm.

Tolerances Listed Under 40 CFR §180.399 (b)

Following evaluation of acceptable livestock metabolism studies, CBRS has determined that the residues to be regulated in livestock should continue to be the parent, its isomer RP-30228, and metabolites RP-32490 and RP-36114 which comprise the current tolerance expression for livestock. With the evaluation that livestock feeding data are acceptable, and with the completion of Phase 5 review of livestock feed items, tolerances can be reassessed for livestock commodities. If an acceptable enforcement method is developed to determine individual tolerance residues rather than common moieties, it may be appropriate to lower tolerance levels for livestock commodities.

Tolerances Listed Under 40 CFR §180.399 ©

Adequate data are available to reassess the established tolerance for Chinese mustard.

Tolerances Listed Under 40 CFR §180.399 (d)(1)

The time-limited tolerance for cottonseed, established under PP#2F4111 (61 FR 19845, 5/3/96), expired on March 15, 1997; therefore, this tolerance can not be reassessed. HED notes that the registrant filed a proposal (62 FR 3691, 1/24/97) for an extension of this time-limited tolerance which was denied.

Tolerances Listed Under 40 CFR §180.31

Temporary tolerances for tangelos and tangerines, established under PP#3G4210, expired in 1997; therefore, these tolerances can not be reassessed. HED notes that the registrant filed a petition proposal (PP#3G4210) for an extension of these temporary tolerances (62 FR 3691, 1/24/97) which was denied.

Tolerances Listed Under 40 CFR §185.3750

There are no processed commodities associated with ginseng (Table 1, OPPTS GLN 860.1000). Therefore, the established food additive tolerance for "ginseng, dried" should be revoked concomitant with the establishment a Section 408 tolerance of 4 ppm for the combined Iprodione residues of concern in/on "ginseng, root, dried". The tolerance for raisins should be changed to 15 ppm.

Tolerances Listed Under 40 CFR §186.3750

The established feed additive tolerances for peanut soapstock, grape dry pomace, and raisin waste should be revoked since these items have been removed from Table 1 (OPPTS GLN 860.1000) because they are not considered to be significant livestock feed items. The Agency has proposed the revocation of the established feed additive tolerance for peanut soapstock (60 FR 49142, 9/21/95).

Current tolerance levels for rice hulls and bran are appropriate.

Pending Tolerance Petitions

PP#4F4281: Rhone-Poulenc has submitted this petition for the establishment of tolerances for the combined residues of Iprodione, its isomer, and one metabolite in/on canola (rape seed). This petition is currently in reject status because of deficiencies pertaining to storage stability and residue data (CB No. 14416, DP Barcode D207414, 4/6/95, M. Flood).

Table 17. Tolerance Reassessment Summary for Iprodione.

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/ *[Correct Commodity Definition]*
Tolerances Listed Under 40 CFR §180.399 (a)			
Almonds, hulls	2.0	2.0	
Almonds, nutmeat	0.3	0.3	[*Almonds, nutmeats*]
Apricots	20.0	20.0	
Beans, dry	2.0	2.0	
Beans, succulent	2.0	2.0	
Beans, dried, vine hay	90.0	Revoke	Provided labels are amended such that Iprodione use on cowpeas is prohibited, these tolerances should be revoked.
Beans, forage	90.0	Revoke	
Blueberries	15.0	15.0	
Boysenberries	15.0	Revoke	Iprodione residues on boysenberries and raspberries are covered by the established tolerance for [*Caneberry (blackberry and raspberry) subgroup*].
Raspberries	15.0	Revoke	
Broccoli	25.0	25.0	
Caneberries	25.0	25.0	[*Caneberry (blackberry and raspberry) subgroup*]
Carrots	5.0	5.0	
Cherries (sour)	20.0	20.0	
Cherries (sweet) (pre- and postharvest)	20.0	20.0	
Currants	15.0	15.0	The available blueberry data can be translated to currants.
Garlic	0.1	0.1	
Ginseng	2.0	Replace	The appropriate RAC for ginseng is dried root (Table 1, OPPTS GLN 860.1000). Concomitant with the revocation of tolerance for "ginseng", a Section 408 tolerance of 4.0 ppm on [*ginseng, root, dried*] should be established.
Grapes	60.0	10.0	
Kiwi fruit	10.0	10.0 [1]	[*Kiwifruits*]
Lettuce	25.0	25.0	
Nectarines (pre- and postharvest)	20.0	20.0	
Onions, dry bulb	0.5	0.5	[*Onions, bulb*]

(*continued: footnotes follow*)

Table 17 *(continued)*.

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/ *[Correct Commodity Definition]*
Peaches (pre- and postharvest)	20.0	0.05	Reassessed tolerance at 0.05 ppm based on voluntary deletion of all post harvest uses and label amendments
Peanuts, nutmeat	0.5	0.5	
Peanut hay	150.0	Revoke	Label amendments to prohibit the feeding of peanut hay to livestock have been submitted.
Peanut forage	150.0	Revoke	These items are no longer considered significant livestock feed items (Table 1, OPPTS GLN 860.1000).
Peanut hulls	7.0		
Plums (pre- and postharvest)	20.0	20.0	
Potatoes	0.5	0.5	
Prunes	20.0	80.0	
Rice grain	10.0	10.0	*[Rice, grain]*
Rice straw	20.0	20.0	*[Rice, straw]*
Strawberries	15.0	15.0	
Tolerances Listed Under 40 CFR §180.399 (b)			
Cattle, fat	0.5	0.5	
Cattle, kidney	3.0	3.0	
Cattle, liver	3.0	3.0	
Cattle, meat	0.5	0.5	
Cattle, meat byproducts (mbyp) (except kidney and liver)	0.5	3.0	
Eggs	1.5	1.5	
Goats, fat	0.5	0.5	
Goats, kidney	3.0	3.0	
Goats, liver	3.0	3.0	
Goats, meat	0.5	0.5	
Goats, mbyp (except kidney and liver)	0.5	3.0	
Hogs, fat	0.5	0.5	
Hogs, kidney	3.0	3.0	
Hogs, liver	3.0	3.0	
Hogs, meat	0.5	0.5	

(continued: footnotes follow)

Table 17 *(continued)*.

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/ *[Correct Commodity Definition]*
Hogs, mbyp (except kidney and liver)	0.5	3.0	
Horses, fat	0.5	0.5	
Horses, kidney	3.0	3.0	
Horses, liver	3.0	3.0	
Horses, meat	0.5	0.5	
Horses, mbyp (except kidney and liver)	0.5	3.0	
Milk	0.5	0.5	
Poultry, fat	3.5	7.0	
Poultry, liver	5.0	7.0	
Poultry, meat	1.0	1.0	
Poultry mbyp (except liver)	1.0	7.0	
Sheep, fat	0.5	0.5	
Sheep, kidney	3.0	3.0	
Sheep, liver	3.0	3.0	
Sheep, meat	0.5	0.5	
Sheep, mbyp (except kidney and liver)	0.5	3.0	
Tolerances Listed Under 40 CFR §180.399 ©			
Chinese mustard	15.0	15.0	[*Mustard, Chinese*]
Tolerance Listed Under 40 CFR §180.399 (d)(1)			
Cottonseed	0.10	N/A, Expired	Tolerance expired in 1997. Therefore, it can not be reassessed at this time.

(*continued; footnotes follow*)

Table 17 *(continued)*.

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/ *[Correct Commodity Definition]*
Tolerances Listed Under 40 CFR §180.31			
Tangelos	3.0	N/A, Expired	Tolerances expired in 1997 and therefore can not be reassessed at this time.
Tangerines	3.0	N/A, Expired	
Tolerances Listed Under 40 CFR §185.3750			
Ginseng, dried	4.0	Revoke	There are no processed commodities associated with ginseng (Table 1, OPPTS GLN 860.1000).
Raisins	300	15.0	
Tolerances Listed Under 40 CFR §186.3750			
Grapes, pomace, dry	225.0	Revoke	These items are no longer considered significant livestock feed items (Table 1, OPPTS GLN 860.1000).
Raisin waste	300.0	Revoke	
Rice bran	30.0	30.0	
Rice hulls	50.0	50.0	
Soapstock	10.0	Revoke	This item is no longer considered a significant livestock feed item (Table 1, OPPTS GLN 860.1000).

[1] Note: There are no U.S. registrations for kiwifruit as of 12/11/96; the currently established tolerance for kiwifruit is an import tolerance.

c. Codex Harmonization

The Codex Alimentarius Commission has established maximum residue limits (MRLs) for Iprodione residues in/on various commodities (see *Guide to Codex Maximum Limits For Pesticide Residues, Part 2, FAO CX/PR, 4/91*). The Codex MRLs are expressed in terms of Iprodione *per se*. Harmonization of the Codex MRLs with the U.S. tolerances is not feasible at this time because of differences in the U.S. tolerance and Codex MRL expressions. Although incompatible, a numerical comparison of the Codex MRLs and the corresponding **reassessed** U.S. tolerances is presented in Table 18.

Table 18. Codex MRLs and applicable U.S. tolerances.

Codex			Reassessed U.S. Tolerance, ppm
Commodity, As Defined	MRL, mg/kg [1]	Step	
Almonds	0.2	5/8	0.3
Apple	10	CXL [2]	--
Barley	2	5/8	--
Beans (dry)	0.2	CXL [2]	2.0
Beans (dry)	0.1	5/8	2.0
Blackberries	30	5	25.0
Broccoli	25	5/8	25.0
Carrot	10	5	5.0
Cherries	10	5	20.0
Common bean (pods and/or immature seeds)	2	5	--
Cucumber	5	CXL [2]	--
Cucumber	2	5/8	--
Currants, Black, Red, White	5	CXL [2]	15.0
Garlic	0.1	CXL [2]	0.1
Grapes	10	CXL [3]	10.0
Kiwifruit	5	CXL [3]	10.0
Lettuce, Head	10	CXL [3]	25.0
Lettuce, Leaf	25	5/8	25.0
Onion, Bulb	0.1	CXL [2]	0.5
Onion, Bulb	0.2	5/8(a)	0.5
Peach (post-harvest treatment)	10	CXL [2]	20.0
Peach	10	5/8(a)	20.0
Pear	10	CXL [2]	-
Peppers, Sweet	5	CXL [2]	-

(*continued; footnotes follow*)

Codex			Reassessed U.S. Tolerance, ppm
Commodity, As Defined	MRL, mg/kg [1]	Step	
Plums (including prunes)	10	CXL [2]	20.0 (prunes, 80.0)
Pome fruits	5	5/8(a)	--
Rape seed	0.5	5/8	--
Raspberries, Red, Black	5	CXL [2]	25.0
Raspberries, Red, Black	30	5/8(a)	25.0
Rice, Husked	3	CXL	Rice grain, 10.0
Rice, Husked	10	5	Rice grain, 10.0
Strawberry	10	CXL	15.0
Sugar beet	0.1 (*)	5/8(a)	--
Sunflower seed	0.5	5/8	--
Tomato	5	CXL [4]	--
Witloof chicory (sprouts)	1	CXL [3]	--

[1] An asterisk (*) signifies that the MRL was established at or about the limit of detection.
[2] Deletion was recommended (1994 JMPR). Where there are multiple entries for the same crop/group, the current MRL will be canceled upon replacement.
[3] Confirmed (1994 JMPR).
[4] Withdrawal was recommended (1994 JMPR); on hold for promised data from France.

d. Dietary Risk Assessment/Anticipated Residues

HED calculated specific anticipated residues for determination of upper bound carcinogenic risk from Iprodione (Abbotts 1996, 2/16/96). It should be noted that some anticipated residues were *higher* than previous estimates (Abbotts 1995a) because residue estimates were refined with additional data from the USDA's Pesticide Data Program (PDP). As part of a previous Dietary Residue Exposure System (DRES) analysis (Wintersteen 1995), anticipated residues based on monitoring data were adjusted for percent crop treated data. BEAD has updated these percent crop treated data (Halvorson 1995) and this analysis reflects the revised values.

1. Exposure and Risk From Food Sources

(a) Acute Dietary Risk (Tier ½/3/4)

Two analyses of acute dietary exposure and risk were performed using DRES, one for all presently registered commodities and one for all commodities proposed for tolerances.

The DRES detailed acute analysis estimates the distribution of single-day exposures for the overall U.S. population and certain subgroups. The analysis evaluates individual food

consumption as reported by respondents in the USDA 1977-78 Nationwide Food Consumption Survey (NFCS) and accumulates exposure to the chemical for each commodity. Each analysis assumes uniform national distribution of Iprodione in the commodity supply.

Acute dietary exposure to Iprodione was estimated by DRES. Acute dietary exposure estimates are considered to be high end, because exposure estimates are based on tolerance level residues in all foods. High end acute dietary exposure was then compared with the acute NOEL of 20 mg/kg/day for Iprodione, and expressed as a margin of exposure (MOE). The Margin of Exposure (MOE) is a measure of how close the high end exposure comes to the NOEL (the highest dose at which no effects were observed in the laboratory test), and is calculated as the ratio of the NOEL to the exposure (NOEL/exposure = MOE).

For Iprodione, the target MOE for acute dietary risk is 300; MOEs above 300 are not considered to be of concern. For Iprodione, the target MOE of 300 includes a 3X uncertainty factor for FQPA considerations. Acute MOEs for Iprodione are calculated for females 13+ only because the toxicological endpoint, decreased anogenital distance, was noted in neonates following in utero exposure to Iprodione.

DRES results for the acute dietary assessment are of concern for both existing and proposed tolerances for Iprodione. Exposure to tolerance level residues on presently registered commodities results in an acute dietary exposure of 0.18 mg/kg/day and an MOE of 111 for females 13+years old (13+). Exposure to tolerance level residues on currently registered commodities and those proposed for tolerances results in an acute dietary exposure of 0.30 mg/kg/day and an MOE of 66. As stated above, the target MOE for Iprodione is 300. As previously noted, this acute dietary (food only) exposure assessment is conservative because it assumes tolerance level residues on all commodities with present or proposed Iprodione tolerances and 100 percent crop treated.

The Registrant submitted an acute Monte Carlo dietary exposure assessment in 1997. This acute Monte Carlo assessment was found to be acceptable for regulatory purposes. The assessment uses the Continuing Survey of Food Intake of Individuals (CSFII) 1989-1992 consumption database as translated by Novigen. This database is acceptable. However, OPP and Novigen used different toxicological endpoints for acute dietary risk assessment. The toxicological endpoints used in the Novigen acute dietary assessment was based upon an acute NOEL of 90 mg/kg/BW/day from a rat teratology study. OPP is using an acute NOEL of 20 mg/kg/day from a special rat teratology study (on sexual differentiation) for acute dietary risk estimates. This NOEL is applied only to females 13+.

The Novigen assessment was highly refined, using a distribution of residue levels for commodities and percent crop treated data in the analysis. Field trial data supplied by Rhone-Poulenc were used for all crops. The field trials selected were appropriately matched to the maximum label rates for Iprodione. **However, it would benefit the Agency by requesting that the registrant identify precisely which field trials were used in the acute Monte Carlo**

submission and supply a rationale for why the particular peach field trials used were selected (as opposed to others available).

MOEs from the Novigen Acute Monte Carlo were recalculated using the EPA NOEL of 20 mg/kg/day. The results of the reanalysis are provided in table 19 along with the results of the acute dietary analysis using HED's Dietary Residue Exposure System (DRES). For the acute Monte Carlo dietary risk assessment, using a NOEL of 20 mg/kg/day, females 13+ have MOEs of less than 300 at the 99.9th percentile of exposure.

Table 19. Acute Dietary Risk as Indicated by Margins of Exposure (MOE)*

Population Subgroup	Dietary Exposure, mg/Kg/day			MOE		
	DRES existing tolerances	DRES proposed tolerances	Monte Carlo 99.9th%tile	DRES existing tolerances	DRES proposed tolerances	Monte Carlo 99.9th%tile
Females 13+	0.18	0.3	0.144024	111	66.6	139

* MOEs from the Novigen Acute Monte Carlo were recalculated using the EPA NOEL (20 mg/kg/day); ** Margin of exposure is the NOEL ÷ the exposure estimate.

(b) Chronic, Non-Carcinogenic Risk (TMRC and ARC)

The total dietary exposure for Iprodione, expressed as % Chronic FQPA RfD, was calculated for Iprodione using the following equation:

$$\% \text{ Chronic FQPA RfD} = \frac{\text{TMRC or ARC mg/kg/day}}{\text{Chronic FQPA RfD of x mg/kg/day}} \times 100\%$$

Exposure from current registered uses of Iprodione results in an estimated risk which represents < 1% of the RfD for all populations.

The chronic analysis for Iprodione is a highly refined estimate of dietary exposure. Refinements such as percent crop treated data and anticipated residues have been incorporated. Based on the risk estimates calculated in this analysis, chronic dietary risk from the uses recommended through Reregistration, does not exceed HED's level of concern.

© Chronic, Carcinogenic Risk (ARC)

The upper bound carcinogenic risk from food uses of Iprodione for the general U.S. population was calculated using the following equation:

Upper Bound Cancer Risk = Dietary Exposure (ARC) x Q_1^*

Based on a Q_1^* of 0.0439 $(mg/kg/day)^{-1}$, the upper bound cancer risk was calculated to be 4×10^{-6} contributed through all the published uses for Iprodione. The overall upper bound risk appears to be above the range the Agency generally considers negligible for excess life time cancer risk. The commodities which contribute the most to this risk figure are stone fruits at 1.4×10^{-6} and small fruits and berries at 1.0×10^{-6}.

The upper bound cancer risk for all commodities with proposed (reassessed) tolerances was calculated to be 6.5×10^{-6} The commodities which contribute the most to this risk figure are grapes (including wine and sherry) at 3.0×10^{-6}, stone fruits at 1.5×10^{-6}, and small fruits and berries at 1.0×10^{-6}. The upper bound cancer risk based on ARC for all commodities with proposed (reassessed) is above the range the Agency generally considers negligible for excess life time cancer risk.

e. Drinking Water Exposure

The Environmental Fate and Effects Division (EFED) has evaluated potential drinking water exposure from Iprodione in ground and surface water.

1. Ground Water (modeling/monitoring)

EFED originally had a concern for Iprodione in groundwater based on modeling results (LEACH, Wolf 1997). However, when EFED conducted a Tier 2 Drinking Water Assessment, they concluded that Iprodione leaching to groundwater is expected to be negligible (Abel 1997b). EFED reviewed readily available groundwater monitoring data for the Tier 2 water assessment. Iprodione has been reported in several small scale studies in areas of the U.S. where it is or is suspected of being used. Impact to ground water source drinking water is expected to be minimal when the known environmental fate and monitoring data, showing all samples below the LOQ, are considered.

From April to October 1996 monitoring in 40 wells along the Oregon coastal region was conducted. Eighty-nine samples were collected, up to four samples at some wells over the period of the study, from the 40 wells. All samples were reported as below the level of quantification (LOQ); 0.1 ppb. No correlation with use areas was established, although samples were collected from areas with known grape production.

In another study along the Central Snake River basin in Oregon, 27 wells were sampled for a total of 30 samples. Iprodione was detected in all samples, but were reported as below the level of

quantification (0.1 ppb) in all samples. The study was conducted during a three day period during August 1996. No correlation with the use of Iprodione was established.

A study conducted in the Lake Superior Western Basin in Wisconsin during July 1995 at two wells reported all samples (5) as below the LOQ of 0.55 ppb. No information on why the samples were collected could be established.

Lastly, the Pesticide In Ground Water Database (*EPA, 1992)* reported one study in Massachusetts during 1986 in which 15 wells were sampled. No samples reported finding Iprodione above or below the maximum contaminant level (MCL).

Monitoring data are limited by the lack of a correlation between sampling date and the use patterns of the pesticide within the drainage basin studied. Also, the monitored wells were not associated with groundwater drinking water sources (Abel 1997b).

2. Surface Water (modeling/monitoring)

Because the tier I drinking water exposure assessment for Iprodione showed exposures of concern (Nelson 1997, Scheltema 1997), EFED conducted a Tier II drinking water exposure assessment. The Tier II assessment for Iprodione uses PRZM 2.3 for simulating the agricultural field and EXAMS 2 for fate and transport in surface water. Spray drift was simulated using the assumption that 1% of applied Iprodione reached surface water at the time of application and 95% of the chemical deposited on the target site. The remaining 4% either remained airborne or deposited on the ground beyond the drainage basin for the pond.

The scenarios chosen for Iprodione were a peach orchard in Peach County, Georgia and a grape vineyard in Chautauqua County, New York. Scenarios were chosen to represent sites that were expected to produce runoff greater than 90% of the sites where the appropriate crop is grown. Model simulations were made with the maximum application rates, maximum number of yearly applications, and the shortest recommended application interval. Tier II upper tenth percentile EECs are presented in Table 21. The EECs have been calculated so that in any given year, there is a 10% probability that the maximum average concentration of that duration in that year will equal or exceed the exposure estimate (EEC) at the site.

The Tier II EECs are based on a high-end exposure scenario for the use of a pesticide on a peaches. The meteorology and agricultural practice are simulated at the site over multiple (in this case, 23-34) years such that the probability of an EEC occurring at that site can be estimated. EECs were calculated for Rovral (Iprodione) as this was the formulation registered for use on the specific crops.

To represent the use on peaches, three applications were made prior to petal fall according to label directions at specific intervals (14 days after first application and again 7 days later) beginning with bud emergence. All applications were assumed to made by ground spray.

On grapes. four applications were made during the growth cycle; at mid-bloom, prior to bunch closing. beginning of fruit ripening, and seven days before harvest. Approximate pesticide application dates in the growth cycle were established with the assistance of the lead viticulturist from the Fredonia Regional Extension Office in New York. All applications were are made by ground spray equipment directly onto the growing plant.

Table 20 . Usage Practice for Modeling Iprodione

Chemical	Crop	Application Method	Application Rate Iprodione (lb acre^{-1})	Maximum Annual Applications	Application Interval
Iprodione	Peaches	Ground Spray	1.0	3	14/7 days.
	Grapes	Ground Spray	2.0	4	Variable

Table 21. Tier II Upper 10th Percentile EECs for Iprodione Use on Peaches and Grapes

Crop	Aerobic Soil Metabol. Rate ($t_{1/2}$)	Estimated EEC's (ug/l)					
		Max.	4 Day	21 Day	60 day	90 Day	Long Term Mean
Peaches	90 Day	14.7	13.8	11.0	8.1	6.7	1.5
Peaches	45 Day	12.7	11.9	9.4	7.2	6.1	1.4
Grapes	90 day	13.0	11.5	10.0	7.6	7.4	2.8
Grapes	45 day	10.3	8.6	5.5	3.6	3.6	1.1

PRZM2.3 is a runoff model, which can estimate the off-site movement of synthetic organic chemicals from agricultural fields over a period of up to 36 years. PRZM2.3 was developed to simulate the transport and transformation of field-applied pesticides in the crop root zone and the vadose zone taking into account the effects of agricultural management practices. It is considered to be appropriate for modeling most agricultural field crops on mineral soils in the US. Using input variables such as pesticide fate properties, soil characteristics, soil/crop management practices, and daily weather, PRZM2.3 can simulate a pesticide's fate and transport in/on soil and plants, leaching to the bottom of the root zone, water runoff and soil erosion. The output that is linked to EXAMS2 includes estimated runoff volume, sediment yield, and associated edge of the field pesticide losses (which constitute pesticide loadings to edge of the field surface water).

Surface water models such as EXAMS2 simulate pesticide fate and transport in surface water and sediment. Input includes runoff volume, and pesticide losses dissolved in runoff water and adsorbed

to eroding soil (from PRZM2.3) as well as pesticide fate properties, and receiving water characteristics. Output includes estimated peak and various average pesticide concentrations dissolved in the water column, adsorbed to suspended sediment, and adsorbed to bottom sediment as a function of time and location.

It should be noted that PRZM2.3/EXAMS2 were designed for use in ecological risk assessment. They are not ideal tools for use in drinking water risk assessment. Drinking water taken from surface water tends to come from bodies of water that are substantially larger than a 1 hectare by 2 meters deep pond. As in the case of the Tier 1 screen, PRZM2.3/EXAMS2 assumes that the entire basin (a 10 hectare field) receives an application of the chemical. In virtually all cases, basins large enough to support a drinking water facility will contain a substantial fraction of area which does not receive the chemical. Furthermore, there is always at least some flow (in a river) or turn over in a reservoir or lake. Pesticide concentrations modeled using PRZM2.3/EXAMS2 represent upper-bound concentrations that may actually occur at the edge of a pond, but not the concentrations that could occur in flowing water. Therefore, PRZM2.3/EXAMS2 should be considered as a screen. PRZM2.3/EXAMS2 over-estimates the actual drinking water concentrations.

There are large uncertainties in extrapolating fate data from laboratory to field, and from field to field. Additionally, several important environmental processes are not adequately simulated such as pesticide uses on turf, and orchards. Screening models such as PRZM2.3/EXAMS2 are best used to determine that a chemical poses little or no exposure. If, a risk assessment performed using an high-end/upper-bound exposure modeled by PRZM2.3/EXAMS2 does not exceed HED's level of concern, then there would be no reason to refine the assessment.

f. Drinking Water Risk

In the absence of reliable, available monitoring data, EFED uses models to estimate concentrations of pesticides in ground and surface water. For Iprodione, modeling was used to estimate surface water concentrations because of very limited surface water monitoring data. However, HED does not use these model estimates to quantify risk. Currently, HED uses drinking water levels of concern (DWLOCs) as a surrogate to capture risk associated with exposure to pesticides in drinking water. A DWLOC is the concentration of a pesticide in drinking water that would be acceptable as an upper limit in light of total aggregate exposure to that pesticide from food, water, and residential uses (if any). A DWLOC will vary depending on the residue level in foods, the toxicity endpoint and with drinking water consumption patterns and body weights for specific subpopulations.

HED did not calculate DWLOC values for cancer and acute dietary endpoints. This is because the effective DWLOC is zero for both acute and cancer dietary exposure, as exposure to Iprodione residues in food alone exceed HED's level of concern for both of these risk estimates. Until the exposure from Iprodione residues in food is reduced, any additional exposure to Iprodione in drinking water would cause acute and cancer dietary risks to further exceed HED's level of concern. HED did calculate DWLOC values for the chronic (RfD) endpoint. HED has compared concentration estimates from the PRZM/EXAMS model to calculated DWLOC values to provide a screening level

(qualitative) risk estimate for Iprodione in surface water. If screening model estimates exceed the DWLOC values, monitoring data may be required.

The equations below were used to calculate the $DWLOC_{chronic}$ based on aggregate exposure to Iprodione through food and drinking water.

*Exposure to Iprodione in drinking water (mg/kg/day) = chronic Rf D - (food exposure + residential exposure)

[* The chronic FQPA RfD is 0.02 mg/kg/day. Food exposure is taken from the chronic DRES analysis for each subpopulations for which a DWLOC value is calculated. Residential exposures equal zero.]

Exposure (adults) (mg/kg/day) = 0.02 mg/kg/day - (0.0002 mg/kg/day + 0) = 0.0198 mg/kg/day

$DWLOC_{chronic}$ for adult males (ug/L) = (0.0198 mg/kg/day) (70 kg) ÷ (2L) (10^{-3} mg/ug) = 693 ug/L

$DWLOC_{chronic}$ for adult females (ug/L) = (0.0198 mg/kg/day) (60 kg) ÷ (2L) (10^{-3} mg/ug) = 594 ug/L

Exposure (child) (mg/kg/day) = 0.02 mg/kg/day - (0.0003 mg/kg/day + 0) = 0.0197 mg/kg/day

$DWLOC_{chronic}$ for child (ug/L) = (0.0197 mg/kg/day) (10 kg) ÷ (1L) (10^{-3} mg/ug) = 197 ug/L

Conservative model estimates of a long-term average concentration of Iprodione in surface water associated with use on peaches and grapes range up to a few parts per billion (1 to 3 ug/L). The estimated concentrations in surface water are much lower than HED's calculated drinking water levels of concern (DWLOCs) for the above subpopulations for chronic exposure and risk assessments.

HED also calculated DWLOC values for the **short-term endpoint** and compared concentration estimates from the PRZM/EXAMS model to calculated DWLOC values to provide a screening level (qualitative) risk estimate for Iprodione in surface water. If screening model estimates exceed the DWLOC values, monitoring data may be required. DWLOC values for short-term risk assessments are calculated below for adults only. Residential handler exposure scenarios for short- and intermediate-term inhalation exposure are not applicable to children. As per OPP's interim guidance on aggregate risk assessments, if an oral endpoint is needed for short-term risk assessment for incorporation of food, water, or oral hand-to-mouth exposures into an aggregate assessment, and only dermal or inhalation endpoints have been selected, the acute oral endpoint is used to incorporate the oral component into the aggregate risk.

*Exposure to Iprodione in drinking water (mg/kg/day) = acute FQPA RfD - (food exposure + residential exposure)

[* The acute FQPA RfD is 0.06 mg/kg/day. Food exposure is taken from the chronic DRES analysis for each subpopulations for which a DWLOC value is calculated. Residential exposures are taken from Table 14. Residential Short- and Intermediate-Term Inhalation Risks at Baseline.]

Exposure (adults) (mg/kg/day) = 0.06 mg/kg/day - (0.0002 mg/kg/day + 0.002 mg/kg/day) = 0.0578 mg/kg/day

$DWLOC_{chronic}$ for adult males (ug/L) = (0.0578 mg/kg/day) (70 kg) ÷ (2L) (10^{-3} mg/ug) = 2000 ug/L

$DWLOC_{chronic}$ for adult females (ug/L) = (0.0578 mg/kg/day) (60 kg) ÷ (2L) (10^{-3} mg/ug) = 1700 ug/L

HED also calculated DWLOC values for the **intermediate-term endpoint** and compared concentration estimates from the PRZM/EXAMS model to calculated DWLOC values to provide a screening level (qualitative) risk estimate for Iprodione in surface water. If screening model estimates exceed the DWLOC values, monitoring data may be required. DWLOC values for intermediate-term risk assessments are calculated below for adults only. Residential handler exposure scenarios for short- and intermediate-term inhalation exposure are not applicable to children. As per OPP's interim guidance on aggregate risk assessments, if an oral endpoint is needed for intermediate-term risk assessment for incorporation of food, water, or oral hand-to-mouth exposures into an aggregate assessment, and only dermal or inhalation endpoints have been selected, the oral endpoint on which the FQPA RfD is based is used to incorporate the oral component into the aggregate risk.

*Exposure to Iprodione in drinking water (mg/kg/day) = chronic FQPA RfD - (food exposure + residential exposure)

[* The chronic FQPA RfD is 0.02 mg/kg/day. Food exposure is taken from the chronic DRES analysis for each subpopulations for which a DWLOC value is calculated. Residential exposures are taken from Table 14. Residential Short- and Intermediate-Term Inhalation Risks at Baseline.]

Exposure (adults) (mg/kg/day) = 0.02 mg/kg/day - (0.0002 mg/kg/day + 0.0017 mg/kg/day) = 0.0181 mg/kg/day

$DWLOC_{chronic}$ for adult males (ug/L) = (0.0181 mg/kg/day) (70 kg) ÷ (2L) (10^{-3} mg/ug) = 633 ug/L

$DWLOC_{chronic}$ for adult females (ug/L) = (0.0181 mg/kg/day) (60 kg) ÷ (2L) (10^{-3} mg/ug) = 543 ug/L

As noted above, conservative model estimates of a long-term average concentration of Iprodione in surface water associated with use on peaches and grapes range up to a few parts per billion (1 to 3 ug/L). The estimated concentrations in surface water are much lower than HED's calculated drinking water levels of concern (DWLOCs) for the above subpopulations for short- and intermediate-term exposure and risk assessments. HED uses average residues in water and food in all aggregate risk assessments, except in the acute aggregate assessment, where high-end food and water residues are used. Since the $DWLOC_{acute}$ is effectively zero and was not calculated, all of the DWLOC values

calculated here have been compared to long-term average concentration estimates from the screening-level models. Model estimates of Iprodione in ground water were not available for comparison to DWLOC values.

5. Food Quality Protection Act Considerations

a. Cumulative Risk for 3,5-Dichloroaniline

Need for Assessment

Section 408(b)(2)(D)(V) requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency believes that "available information" in this context might include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments.

Although at present the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments, there are pesticides as to which the common mechanism issues can be resolved. These pesticides include pesticides that are toxicologically dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case common mechanism of activity will be assumed).

Iprodione is structurally related to Vinclozolin and procymidone, which belong to the imide class. Each of these three pesticides can metabolize to 3,5-dichloroaniline (3,5-DCA). FQPA requires HED to estimate cumulative risk from consumption of food and water containing 3,5-DCA derived from Iprodione, Vinclozolin, and procymidone. This was previously done in conjunction with the Vinclozolin RED of July 15, 1997.

Hazard Identification for 3,5-DCA

3,5-DCA is not a registered pesticide; therefore, there are no FIFRA toxicology data for this compound. In the past, HED has used the Q_1^* for p-chloroaniline (PCA) to assess the carcinogenic risk for other structurally related chloroanilines. The HED policy on chloroanilines specifies that chloroaniline metabolites should be considered to be toxicologically equivalent to PCA unless there is sufficient evidence that the metabolite is not carcinogenic.

A Q_1^* of 6.38×10^{-2} $(mg/kg/day)^{-1}$ in human equivalents has been calculated for p-chloroaniline. This Q_1^* is based on the spleen sarcoma rate in male rats from an NTP bioasssay, linearized low dose multistage model, and the 3/4s interspecies scaling factor (Fisher 1994).

Exposure Assessment

Exposure to 3,5-DCA will be evaluated from the following sources: residues of Iprodione- and Vinclozolin-derived 3,5-DCA in food, residues of procymidone-derived 3,5-DCA in imported wine, and 3,5-DCA residues in water from agricultural use of Iprodione and Vinclozolin. There are no US registrations for procymidone; therefore, an evaluation of exposure to procymidone-derived 3,5-DCA in water is not appropriate.

(I). Iprodione-derived 3,5-DCA residues in food

Metabolism data submitted to fulfill guideline requirements for the re-registration of Iprodione indicated that 3,5-DCA represented 1% total radioactive residue (TRR) in eggs, smaller proportions in other livestock commodities, and was not detected in primary or rotational crops. One percent of the Iprodione residues as estimated in a chronic DRES analysis (US population) would be appropriate values for use in an assessment for 3,5-DCA.

A chronic DRES analysis for Iprodione was completed on April 24, 1998 (Steinwand 1998b). This analysis used highly refined anticipated residues. The estimated exposure to Iprodione residues for total red meat was 0.002668 ug/kg/day, for total poultry was 0.001999 ug/kg/day, and for total dairy (milk and eggs) was 0.004552 ug/kg/day. The estimated exposure for 3,5-DCA derived from Iprodione in food is calculated as follows:

(Iprodione exposure, ug/kg/day)(0.001mg/ug)(1% TRR as 3,5-DCA) =3,5-DCA exposure, mg/kg/day.

The total estimated exposure to Iprodione-derived 3,5-DCA in food is 0.00000009219 mg/kg/day.

(ii). Vinclozolin-derived 3,5-DCA residues in food

Metabolism data submitted to fulfill Reregistration guideline requirements for Vinclozolin indicated that DCA represented 9.6% TRR in peaches, smaller proportions in strawberries and was not detected in lettuce or grapes. Therefore, HED is assuming that 10% Vinclozolin residues as estimated in a chronic DRES analysis would be appropriate values for use in an assessment for 3,5-DCA. Wine is included in the analysis because the metabolism studies for procymidone showed that the 3,5-DCA metabolite is formed in wine even though it is not detected in grapes.

A chronic DRES analysis for Vinclozolin was performed in 1997 with refined anticipated residue values was performed (Steinwand 1997). The total anticipated residue contribution is 0.143224 ug/kg/day. The estimated exposure for 3,5-DCA derived from Vinclozolin in food can be calculated as follows:

(Vinclozolin exposure, ug/kg/day)(0.001mg/ug)(10% TRR as 3,5-DCA) =3,5-DCA mg/kg/day.

The total estimated exposure to Vinclozolin derived 3,5-DCA in food is 0.0000143224 mg/kg/day.

(iii). Procymidone-derived 3,5-DCA Residues in Wine

The tolerance for procymidone is for imported wine only. The 3,5-DCA metabolite was not detected in grapes, but occurs during fermentation. An HED review recommended anticipated residues in wine at 0.3 ppm for parent procymidone, and 0.06 ppm for its 3,5-DCA metabolite.

Using the equation described in a procymidone dietary risk assessment (Willet 199-), the estimated exposure to 3,5-DCA is calculated as follows:

$$\frac{(0.06\text{ ppm 3,5-DCA in wine})(14.5\%\text{ imported wine})(20\%\text{ crop treated})(8\text{ oz wine/day})(29.57\text{ g/oz})(0.001\text{ g/kg})}{70\text{ kg}}$$

= 3,5-DCA exposure

The estimated exposure to procymidone-derived 3,5-DCA in wine is 0.0000058 mg/kg/day.

(iv). 3,5-DCA Residues in Water from Iprodione

A Tier 2 EEC (Estimated Environmental Concentration) was estimated for 3,5-DCA from the degradation of Iprodione as applied to peaches. For Tier 2, two models, PRZM2.3 and EXAMS2, are used to estimate concentrations of pesticide contaminants in surface water. PRZM2.3 (Pesticide Root Zone Model) can be linked to EXAMS2 (Exposure Analysis Modeling System) for a direct transfer of data.

Using PRZM 2.3 for simulating the transport of the pesticide off the agricultural field and EXAMS 2 for fate and transport of the chemical in surface water, EFED estimated the concentration of Iprodione in surface water as a result of an application to peaches for a chronic Exposure to be 1.5 ppb.

However, it is possible to refine this assessment by assuming that only some of the Iprodione converts to 3,5-DCA. A soil photolysis study indicates that a value of 30% (the highest percentage found in any of the studies examined) would be reasonable to account for the Iprodione that is actually converted to 3,5-DCA. Thus, the concentration of 3,5-DCA can be estimated as follows:

(1.5 ppb Iprodione)(0.3) = 0.45 ppb 3,5-DCA in surface water

(v). 3,5-DCA Residues in Water from Vinclozolin

The GENEEC (GENeric Expected Environmental Concentration) program was used to calculate the concentrations used in the drinking water assessment. GENEEC estimates expected concentrations from a few basic chemical parameters and pesticide label application information. GENEEC is a Tier 1 model which uses a chemical's soil/water partition coefficient and degradation half-life values to

estimate runoff from a ten hectare agricultural field into a one hectare by two meter deep pond. GENEEC considers reduction in dissolved pesticide concentration due to adsorption of pesticide to soil or sediment, incorporation, degradation in soil before wash off to a water body, direct deposition of spray drift into the water body, and degradation of the pesticide within the water body.

It should be noted that GENEEC was designed for use in ecological risk assessment. GENEEC is not an ideal tool for used in drinking water risk assessment. Drinking water taken from surface water tends to come from bodies of water that are substantially larger than a 1 hectare by 2 meters deep pond. Furthermore, GENEEC assumes that the entire basin (a 10 hectare field) receives an application of the chemical. In virtually all cases, basins large enough to support a drinking water facility will contain a substantial fraction of area which does not receive the chemical. Furthermore there is always at least some flow (in a river) or turn over in a reservoir or lake. Also, GENEEC is only modeled for time periods of less than one year. Thus, GENEEC should be considered as a screen, since GENEEC could substantially over-estimate the actual drinking water concentrations.

Conservative screening models such as GENEEC are best used to determine that a chemical poses little or no Exposure, but cannot adequately determine whether a chemical is likely to pose high exposures from surface water. GENEEC results showing low concentrations of a chemical can eliminate concern for drinking water Exposure via surface water. If, a risk assessment performed using an estimated concentration modeled by GENEEC does not exceed HED's level of concern, then there would be no reason to refine the assessment.

A Tier 1 EEC (Estimated Environmental Concentration) was calculated for 3,5-DCA from the degradation of Vinclozolin as applied to peaches. Peaches were chosen as the crop for modeling because they represent a high use scenario for Vinclozolin. EFED estimated the concentration of Vinclozolin in surface water as a result of an application on peaches for a chronic Exposure to be 2.6 ppb. However, 20% is the maximum of the parent Vinclozolin that would be expected to convert to 3,5-DCA, based on a field dissipation study which was extrapolated to water.

Thus, (2.6) (0.2) = 0.52 ppb 3,5-DCA in surface water

Cumulative Risk from all sources of 3,5-DCA

The carcinogenic risks are estimated by multiplying the dose by the Q_1^*, 6.38 X 10^{-2} $(mg/kg/day)^{-1}$. Note that under current OPP policy water risks for 3,5-DCA are not quantified. However, for 3,5-DCA the total risk from consumption of food and wine containing residues of Iprodione, Vinclozolin, and procymidone is greater than the FQPA standard of 1 x 10^{-6}. Thus, estimation of an drinking water level of concern is not possible, and would in fact have yielded a negative number. The drinking water risk was quantified merely to demonstrate the magnitude of the risk from drinking water versus the risk from food sources.

Table 22: Estimated Excess Cancer Risk Values for 3,5-DCA		
Route of Exposure	Exposure, mg/kg/day	Excess Cancer Risk Estimate
Iprodione-derived DCA in food	0.00000009219.	6.0×10^{-9}
Vinclozolin-derived DCA in food**	0.0000143224	9.1×10^{-7}
procymidone-derived DCA in wine	0.0000058	3.7×10^{-7}
Total 3,5-DCA in Food and Wine only		1.3×10^{-6}

* The risk for procymidone is weighted by the ratio 52/70 which assumes that wine is not consumed during the first 18 years of a 70 year lifetime. **The values in this table for Vinclozolin-derived DCA in food will be revised as the registrant has deleted the uses on which the Exposure assessment was based (peaches and grapes and a Q_1* for DCA will be used for the risk assessment. The values in this table are based on a Q_1* for PCA).

The total carcinogenic risk for consumption of food and wine containing residues of 3,5-DCA as a result of applications of Iprodione, Vinclozolin, and procymidone is 1.3×10^{-6}. This can be considered to be an over-estimate. Metabolism studies for Iprodione and Vinclozolin were used to estimate the amount of 3,5-DCA present in various commodities by using TRRs to convert Iprodione or Vinclozolin exposures to 3,5-DCA exposures. There is an uncertainty to the risk estimate in that a surrogate Q_1^* is being used for 3,5-DCA. However, due to the structural similarities of 3,5-DCA and PCA, HED believes that for 3,5-DCA, the use of the PCA Q_1^* represents an upper-bound. These are the best risk numbers that can be estimated by HED.

Due to the national nature of the US distribution of food, the dietary (food and wine) carcinogenic assessment can be considered to be a national assessment. However, for pesticides, estimating a national drinking water Exposure is not appropriate. If actual monitoring data for 3,5-DCA as a result of application of either Vinclozolin or Iprodione existed, the concentrations detected would differ from region to region. (This is expected for pesticides due to restrictions on uses for specified crops or restrictions on use in certain geographic areas.) Thus, the amount of 3,5-DCA ingested in drinking water varies from region to region. If a national drinking water Exposure were to be calculated for 3,5-DCA as a result of application of either Vinclozolin or Iprodione, then detections from use areas would be averaged in with non-detections from non-use areas, thus under-estimating potential exposures.

Because drinking water data on DCA residues in water are not available, HED compared the conservative screening-level model estimates of Iprodione concentrations in surface water to drinking water levels of concern (DWLOCs) for DCA. Because the cancer risk estimate for 3,5-DCA derived

from food and wine is 1.3×10^{-6}, the $DWLOC_{cancer}$ is effectively zero (0). Conservative model estimates indicate concentrations of 3,5-DCA of 0.4 to 0.5 ppb.

b. Aggregate Exposure and Risk Assessment/Characterization

Aggregate Exposure and risk is estimated by combining dietary (food and water) and residential exposures.

1. Acute Aggregate Risk

Current HED policy is to include exposures to Iprodione residues in food and water only to calculate the aggregate acute dietary risk. However, HED notes that Exposure to Iprodione residues in food alone exceed HED's levels of concern for acute dietary risk. At this point in time and until the Exposure to Iprodione in the diet is reduced or a more refined acceptable risk assessment is provided, any additional Exposure to Iprodione through drinking water would only cause acute risk estimates to further exceed HED's level of concern. In effect, the drinking water level of concern (DWLOC) for acute effects of Iprodione is zero (0). Although Iprodione uses are not expected to impact ground water (available monitoring data show levels at or below limits of quantification and detection), upper bound estimates of Iprodione in surface waters from conservative screening models indicate concentrations of a few parts per billion.

2. Chronic Aggregate Risk

The chronic aggregate risk assessment for Iprodione will include risk estimates associated with dietary Exposure through food, water, and registered residential uses. Anticipated residues and percent crop-treated data for commodities with published tolerances result in an Exposure to Iprodione through food which represents up to 1.6% of the chronic FQPA RfD for the most exposed subpopulation in the U.S. (non-nursing infants , <1 year old). Exposure to all other groups is less than or equal to 1% of the chronic FQPA RfD.

HED has calculated drinking water levels of concern (DWLOCs) for chronic Exposure to Iprodione from commodities with published tolerances in drinking water for the following four subpopulations: the general U.S. population/Hispanics (690 ppb), females, 13-19 years old (590 ppb), and non-nursing infants, <1 year old (197 ppb). These subpopulations were selected because they contain the individuals believed to be those most highly exposed subpopulations representing males, females, and children and infants, respectively. A conservative estimate (tier 1) of average concentrations of Iprodione in surface water is 1 to 3 ppb. The estimated average concentration of Iprodione in surface water is less than HED's levels of concern. Therefore, based on the risk assessments calculated in this analysis, it appears that the chronic aggregate risk from Iprodione in the diet and drinking water (no residential use scenario was identified for chronic exposure) associated with registered uses of Iprodione is not of concern. Estimated average concentrations of Iprodione in ground water were not available for comparison against DWLOC values; however, based on Iprodione's physical/chemical characteristics and available, but limited monitoring data, it is not expected to impact ground water.

No chronic Exposure scenarios for residential uses of Iprodione were identified: therefore, no chronic Exposure was included in the aggregate risk estimate.

Therefore, based on the available information, HED concludes with reasonable certainty that residues of Iprodione in drinking water (when considered along with Exposure from food and residential uses) would not result in an unacceptable chronic aggregate human health risk estimate at this time. HED bases this determination on a comparison of estimated concentrations of Iprodione in surface water to back-calculated "levels of concern" for Iprodione in drinking water. The estimate of Iprodione in surface water is derived from a water quality model that uses conservative assumptions (health-protective) regarding the pesticide transport from the point of application to surface water. Because HED considers the aggregate risk resulting from multiple Exposure pathways associated with a pesticide's uses, levels of concern in drinking water may vary as those uses change. If new uses are added in the future, HED will reassess the potential impacts of Iprodione on drinking water as a part of the aggregate risk assessment process.

Once concentration estimates of Iprodione in ground water become available, they should be compared to the aforementioned DWLOC values to determine if the estimates exceed the DWLOC values.

3. Cancer Aggregate Risk

Because individual cancer risk estimates for exposures to Iprodione residues through food and residential uses each exceed HED's level of concern individually, combined exposures through these routes results in an aggregate risk that further exceeds HED's level of concern. Any additional Exposure through water would cause the risk estimate to further exceed HED's level of concern. Effectively, the DWLOC for cancer is zero (0). Combined Exposure and risk estimates for each of the residential Exposure scenarios plus dietary Exposure to Iprodione residues results in cancer risk estimates that are all equal to or greater than 10^{-6}. Individual risks associated with dietary Exposure and residential exposures must be reduced before additional Exposure through drinking water would be acceptable. Aggregate exposures from combined inhalation and dermal exposures and the resultant cancer risk estimates for Iprodione are given in Table 23.

4. Short-term Aggregate Risk

Aggregate risk estimates associated with short-term risk includes exposures to average residues of Iprodione in the diet (food and water) and inhalation Exposure (1 to 7 days in duration) through the residential application of Iprodione. The default assumptions used in this aggregate risk estimate are that the homeowner's inhalation Exposure to Iprodione is equivalent to an oral Exposure (100% absorption of the inhaled residues) and the acute oral endpoint (acute FQPA RfD of 0.06 mg/kg/day) was used to incorporate dietary exposures into the aggregate assessment. (As per OPP's interim guidance on aggregate risk assessments, if an oral endpoint is needed for short-term risk assessment for incorporation of food, water, or oral hand-to-mouth exposures into an aggregate assessment, and only dermal or inhalation endpoints have been selected, the acute oral endpoint is used to incorporate the oral component into the aggregate risk.) The toxic endpoint selected for the short-term risk assessment for

exposures to Iprodione through inhalation is the acute oral endpoint also selected for the acute dietary risk assessment, i.e., the acute FQPA RfD. Therefore, the aggregate short-term risk assessment was based on the acute FQPA RfD. The uncertainty factor for both the acute dietary and the short-term inhalation risk assessments is 300. The aggregate risk assessment includes exposures to average concentrations of Iprodione residues in the diet from commodities with existing tolerances, and the high-end Exposure scenario associated with homeowners applying Iprodione with a belly grinder to a lawn. The resulting risk represents 3.6% of the acute FQPA RfD for the U.S. population representing the most exposed population of adult males and females. It is assumed that children and infants do not apply pesticides. Although average residues of Iprodione in drinking water were not available, DWLOCs for this short-term aggregate risk assessment were calculated. They were: for the U.S. population (2000 ppb), and for females representing women 13+ years of age and nursing (1700 ppb). As stated above, based on the available information on Iprodione's impact on surface and ground water, HED believes that Iprodione's impact on drinking water will not affect the aggregate short-term risk significantly. Therefore, HED concludes with reasonable certainty that residues of Iprodione in drinking water (when considered along with Exposure from food and residential uses) would not result in an unacceptable short-term aggregate human health risk estimate at this time. Any change in use pattern would necessitate a reassessment of Iprodione risk estimates.

5. Intermediate-term Aggregate Risk

Aggregate risk estimates associated with intermediate-term risk includes exposures to average residues of Iprodione in the diet (food and water) and inhalation Exposure (7 days to several months in duration) through the residential application of Iprodione. The default assumptions used in this aggregate risk estimate are that the homeowner's inhalation Exposure to Iprodione is equivalent to an oral Exposure (100% absorption of the inhaled residues) and the chronic oral endpoint (chronic FQPA RfD of 0.02 mg/kg/day) was used to incorporate dietary exposures into the aggregate assessment. The toxic endpoint selected for the intermediate-term risk assessment for exposures to Iprodione through inhalation is the chronic oral endpoint also selected for the chronic dietary risk assessment, i.e., the chronic FQPA RfD. Therefore, the aggregate intermediate-term risk assessment was based on the chronic FQPA RfD. The uncertainty factor for both the chronic dietary and the intermediate-term inhalation risk assessments is 300. The aggregate risk assessment includes exposures to average concentrations of Iprodione residues in the diet from commodities with existing tolerances, and the high-end Exposure scenario associated with homeowners applying Iprodione with a belly grinder to a lawn. The resulting risk represents 9.5% of the chronic FQPA RfD for the U.S. population representing the most exposed population of adult males and females. It is assumed that children and infants do not apply pesticides. Although average residues of Iprodione in drinking water were not available, DWLOCs for this intermediate-term aggregate risk assessment were calculated. They were: for the U.S. population (630 ppb), and for females representing women 13+ years of age and nursing (540 ppb). As stated above, based on the available information on Iprodione's impact on surface and ground water, HED believes that Iprodione's impact on drinking water will not affect the aggregate intermediate-term risk significantly. Therefore, HED concludes with reasonable certainty that residues of Iprodione in drinking water (when considered along with Exposure from food and residential uses) would not result in an unacceptable intermediate-term aggregate human health risk estimate at this time. Any change in use pattern would necessitate a reassessment of Iprodione risk estimates.

Table 23. Aggregate Dietary and Residential Handlers Exposure and Cancer Risk Estimates for Iprodione								
Residential Exposure Scenario	Range of Application Rates lb ai/A	Crop Type or Target	Baseline Total Daily Dose mg/kg/day	Number of Exposures per Year	LADD mg/kg/day from residential Exposure	Dietary ARC mg/kg/day	Combined LADD mg/kg/day diet + residential	Cancer Risk
Residential Handler Risk								
Mixing/Loading/Applying Sprays with a Low Pressure Handwand (1)	0.0026 lb ai/gal	Fruit/Nut Trees	0.00093	4	5.1E-6	9.13E-5	9.6E-5	4.2E-6
	0.01 lb ai/gal	Ornamentals	0.0036	4	2.0E-5	9.13E-5	1.1E-4	4.8.0E-8
	0.125 lb ai/ 1,000 ft^2	Turf	0.18	2	5.2E-4	9.13E-5	6.1E-4	2.7E-5
	0.104 lb ai/gal	Vegetable/ Small Fruit Garden	0.037	4	2.0E-4	9.13E-5	2.9E-4	1.3E-5
Mixing/Loading/Applying Using a Backpack Sprayer (2)	0.0026 lb ai/gal	Fruit/Nut Trees	0.000053	4	2.9E-7	9.13E-5	9.2E-5	4.0E-6
	0.01 lb ai/gal	Ornamentals	0.00021	4	1.2E-6	9.13E-5	9.2E-5	4.0E-6
	0.125 lb ai/ 1,000 ft^2	Turf	0.010	2	2.7E-5	9.13E-5	1.2E-4	5.2E-6
	0.104 lb ai/gal	Vegetable/ Small Fruit Garden	0.0021	4	1.2E-5	9.13E-5	1.0E-4	4.5E-6
Mixing/Loading/Applying Using a Garden Hose-end Sprayer (3)	0.0026 lb ai/gal	Trees	0.0028	4	1.6E-5	9.13E-5	1.1E-4	4.7E-6
	0.01 lb ai/gal	Ornamentals	0.011	4	6.0E-5	9.13E-5	1.5E-4	6.6E-6
	0.125 lb ai/ 1,000 ft^2	Turf	0.054	2	1.5E-4	9.13E-5	2.4E-4	1.0E-5

Table 23. Aggregate Dietary and Residential Handlers Exposure and Cancer Risk Estimates for Iprodione								
Residential Exposure Scenario	Range of Application Rates lb ai/A	Crop Type or Target	Baseline Total Daily Dose mg/kg/day	Number of Exposures per Year	LADD mg/kg/day from residential Exposure	Dietary ARC mg/kg/day	Combined LADD mg/kg/day diet + residential	Cancer Risk
Residential Handler Risk								
	0.104 lb ai/gal	Vegetable/ Small Fruit Garden	0.11	4	6.0E-4	9.13E-5	6.9E-4	3.0E-5
Loading/Applying Granulars Using a Belly Grinder (4)	0.0941 lb ai/ 1,000 ft^2	Turf	0.16	2	4.4E-4	9.13E-5	5.3E-4	2.3E-5
	0.0941 lb ai/ 1,000 ft^2		0.0073	2	2.0E-5	9.13E-5	1.1E-4	4.9E-6

Loading/Applying Granulars by Hand as a Spot Treatment (6)	0.0941 lb ai/ 1,000 ft^2	Turf	0.029	2	7.9E-5	9.13E-5	1.7E-4	7.5E-6

Table 23. Aggregate Dietary and Residential Handlers Exposure and Cancer Risk Estimates for Iprodione								
Residential Exposure Scenario	Range of Application Rates lb ai/A	Crop Type or Target	Baseline Total Daily *Dose* mg/kg/day	Number of Exposures *per Year*	LADD mg/kg/day *from* residential Exposure	Dietary ARC *mg/kg/day*	Combined LADD *mg/kg/day* diet + residential	Cancer Risk
Residential Handler Risk								
Loading/Applying Granulars Using a Push-type Lawn Spreader (5)	0.0941 lb ai/ 1,000 ft^2		0.0041	2	1.1E-5	9.13E-5	1.0E-4	4 5-6

	0.0941 lb ai/ 1,000 ft²		0.00021	2	5.8E-7	9.13E-5	9.2E-5	4.0E-6

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c. Endocrine Disruption

Th available toxicology data for Iprodione suggest that it is associated with endocrine effects. However, the extent of these effects and the mode of action are not yet fully understood.

Rhone-Poulenc, the Iprodione Registrant has proposed that the mode of action for the production of Leydig cell tumors by Iprodione is disruption of testosterone biosynthesis. The proposed mode of action and the supporting data have been discussed previously in this document. This proposed mode of action is not fully understood at this time.

Also, a special rat developmental toxicity study with Iprodione showed decreased anogenital distance (AGD) at the mid and high dose level (120 and 250 mg/kg/day). However, there were only marginal differences in AGD between the dose levels.

Last, Iprodione is structurally related to Vinclozolin and Procymidone, which are associated with endoc .

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect..." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1999) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disruptor effects.

III. RISK MANAGEMENT AND REREGISTRATION DECISION

A. Use Pattern/Labeling Rationale/ Dietary Risk Mitigation Measures
B. Occupational and Residential Labeling Rationale/Risk Mitigation Measures

TO BE DETERMINED AFTER RISK MITIGATION DISCUSSIONS WITH REGISTRANTS

IV. ACTIONS REQUIRED BY REGISTRANTS

A. Additional Generic Data Requirements

1. Toxicology Studies

There are no data gaps for the standard Subdivision F Guideline Requirements for a food-use chemical by 40 CFR Part 158. However, the 1994 RfD Committee recommended a postnatal developmental toxicity study in rats due to the close structural similarity of Iprodione to Vinclozolin and because of the effects seen in the reproductive system of male rats as well as in the adrenal glands of both sexes of rats in the combined chronic toxicity/ carcinogenicity study. In response to the above recommendation, the Registrant in 1997 submitted a special study that

examined the sex differentiation of offspring from in pregnant rats exposed orally to Iprodione (MRID No. 44365001).

The 1998 Hazard Identification Review Committee (HIARC) determined that there are outstanding questions with regard to postnatal Exposure that remain to be addressed in light of the observed effects of Iprodione on the testes and its proposed mode of action (disruption of testosterone biosynthesis). Iprodione has been shown to alter anogenital distances in male fetuses following Exposure during late gestation and there is evidence of toxicity to the male reproductive organs in chronic studies in rats. Also, no data are available on the effect of Iprodione on sperm count, motility or morphology in rat or other species. Therefore, the HIARC concluded that an assessment of effects on the male reproductive system following pre and/or postnatal Exposure is required and these aspects can be addressed by conducting the study as described in OPPTS 870.3800

2. Chemistry Studies

a. Product Chemistry

Data are still required on density of the TGAI. Data are required for a new requirement concerning UV/visible absorption for the PAI (OPPTS 830.7050). All other pertinent data requirements are satisfied for the Iprodione 95% T/TGAI. Provided that the registrant submits the data required in the attached data summary table for the 95% T, and either certifies that the suppliers of beginning materials and the manufacturing process for the Iprodione TGAI have not changed since the last comprehensive product chemistry review or submits a complete updated product chemistry data package, CBRS has no objections to the Reregistration of Iprodione with respect to product chemistry data requirements.

b. Residue Chemistry

As noted above, data requirements for rotational crops remain outstanding. CBRS previously advised that depending on crops and plantback intervals chosen, residues in rotational crops would be expected to increase dietary Exposure to Iprodione residues (CBRS 16553, 4/17/96, J. Abbotts). During review of a petition for use on cotton, CBTS required that rotations be restricted to those crops for which primary Iprodione tolerances were already established (PP 2F04111, CBTS 15214, 8/11/95, N. Dodd). CBRS advises that a similar restriction on all Iprodione labels, with obvious exceptions for crops that are not normally rotated, should have the effect of confining dietary risk.

3. Occupational/Residential Exposure Studies

a. Handler Studies

Data gaps exist for the following scenarios:

- (9) - no chemical specific or PHED baseline data exist for applying with a low pressure/high volume handgun to turfgrass.
- (16)- no chemical specific or PHED data exist for mixing/loading/applying as a seed soak treatment.
- (17) - no chemical specific or PHED data exist for mixing/loading/applying as a commercial seed treatment in slurry form.
- (18) - no chemical specific or PHED data exist for mixing/loading/applying solution as a dip treatment.

b. Post-Application Studies

TO BE COMPLETED AT A LATER DATE, FOLLOWING RISK MITIGATION DISCUSSIONS WITH REGISTRANT.

B. Labeling Requirements for End-Use Products

TO BE COMPLETED AT A LATER DATE, FOLLOWING RISK MITIGATION DISCUSSIONS WITH REGISTRANT.

1. Personal Protective Equipment (PPE) and Engineering Control Requirements for Pesticide Handlers
    a. Engineering Control Requirements for Occupational Handlers
    b. PPE Requirements for Occupational Handlers

2. Post-Application/Entry Restrictions
    a. Post-Application Restrictions for WPS Occupational Uses
        1) REI
        2) Early-entry PPE
        3) Double notification
    b. Post-Application Restriction for NonWPS Occupational Uses

3. Application Restrictions
    a. Occupational Products
    b. Homeowner Products

4. Engineering Control Statements for Occupational Products

5. User Safety Statements
    a. User Safety Requirements
        1) Occupational Products
        2) Homeowner Products

    b. User Safety Recommendations
        1) Occupational Products
        2) Homeowner Products

6. Skin Sensitization Statements
    a. Occupational Products
    b. Homeowner Products

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APPENDIX I: REREGISTRATION DATA REQUIREMENTS FOR IPRODIONE

TABLE A **PRODUCT CHEMISTRY DATA SUMMARY**

Guideline Number	Requirement	Are Data Requirements Fulfilled? [1]	MRID Number [2]
830.1550	Product Identity and Disclosure of Ingredients	Y	41790801
830.1600	Starting Materials and Manufacturing Process	Y	41790801
830.1620			
830.1650			
830.1670	Discussion of Formation of Impurities	Y	41790801
830.1700	Preliminary Analysis	Y	**41855501**
830.1750	Certification of Ingredient Limits	Y	**41855501**, CSF 3/12/93 [3]
830.1800	Analytical Methods to Verify the Certified Limits	Y	**41855501**, 42698201 [3]
830.6302	Color	Y	**41855501**
830.6303	Physical State	Y	**41855501**
830.6304	Odor	Y	**41855501**
830.6313	Stability	Y	41958501 [4]
830.7000	pH	N/A [5]	
830.7050	UV/Visible Absorption	N [6]	
830.7200	Melting Point/Melting Range	Y	41570801 [7], **41855501**
830.7220	Boiling Point/Boiling Range	N/A [8]	
830.7300	Density/Relative Density/Bulk Density	N	41517601 [9]
830.7370	Dissociation Constant in Water	N/A [5]	
830.7550	Partition Coefficient (Octanol/Water)	Y	42533601 [10]
830.7560			
830.7570			
830.7840	Solubility	Y	**41855502**
830.7860			
830.7950	Vapor Pressure	Y	41230502, 41230503 [11]

[1] Y = Yes; N = No; N/A = Not Applicable.

[2] Underlined references were reviewed under CBRS No. 8863, D170343, 2/4/92, S. Funk; **bolded** references were reviewed under CBRS No. 9943, D165907, 9/9/92, R. Perfetti; and all other references were reviewed as noted.

[3] CBRS No. 11630, D189537, 9/10/93, R. Perfetti.

[4] CBRS No. 9165, D172676, 6/9/92, S. Funk.

[5] Data are not required because the T/TGAI is not dispersible in water.

[6] The OPPTS Series 830, Product Properties Test Guidelines require data pertaining to UV/visible absorption for the PAI.

[7] CBRS No. 8908, D170539, 1/13/92, K. Dockter.

[8] Data are not required because the T/TGAI is a solid at room temperature.

[9] CBRS No. 17762, D233155, 2/19/97, J. Abbotts: Data were submitted on the PAI; data on the TGAI are required.

[10] CBRS No. 11581, D189210, 6/4/93, F. Toghrol.

[11] CBRS No. 17763, D233154, 2/19/97, J. Abbotts.

APPENDIX II: TABLE B: TOXICOLOGY DATA REQUIREMENTS

Table B. Toxicology Data Requirements for Iprodione				
Guideline	Study Type	MRID #	Required	Satisfied
81-1	acute oral - rats	42306301	yes	yes
81-2	acute dermal - rabbits	40567601	yes	yes
81-3	acute inhalation - rats	42946101	yes	yes
81-4	primary eye irritation	41867301	no	yes
81-5	primary dermal irritation	41867302	no	yes
81-6	dermal sensitization	40567602 42524601	no	yes
81-7	acute delayed neurotoxicity - hen	-	no	no
81-8	acute neurotoxicity - rat	-	no	no
82-1	subchronic feeding - rats	42960701	yes	yes
82-1	subchronic feeding - dog	00157377 00157378 00232702	yes	yes
82-2	21-day dermal - rabbits	42023201	yes	yes
82-5	subchronic neurotoxicity - rats	-	no	no

83-1(a)	chronic toxicity - rats	00071997 00128931 00164249 42637801 42787001	yes	yes
83-1(b)	chronic toxicity - dog	00144391 41327001 42211101	yes	yes
83-2	carcinogenicity - mice	00070963 42825002	yes	yes
83-3(a)	developmental toxicity - rat	00162984 40514901	yes	yes
83-3(b)	developmental toxicity - rabbits	00155469	yes	yes
83-4	2-generation reproduction - rats	00162983 41871601	yes	yes
83-5	chronic toxicity/carcinogenicity - rat	42637801 42787001	yes	yes

84-2	mutagenicity	41604106 00148207 00148208 00148209 43535001	yes	yes
85-1	metabolism	41346701 42984101 43484901	yes	yes
85-2	dermal penetration	43535003	yes	yes
86-1	domestic animal safety	-	no	no
none	mechanism - testes	43535002 43830601 44171901 44171903 44171904	-	-
none	mechanism - liver	44171902	-	-

APPENDIX III: IPRODIONE EPS WITH FOOD/FEED USES

Table C. Iprodione EPs with Food/Feed Uses Registered to Rhone-Poulenc.

EPA Reg. No.	Label Acceptance Date	Formulation	Product Name
264-453 [1]	12/18/96	50% WP	Rovral® Fungicide
264-482 [2]	12/18/96	4 lb/gal FlC	Rovral® 4 Flowable Fungicide
264-520	3/23/94	4 lb/gal FlC	Rovral® R Flowable Fungicide
264-524	12/18/96	50% DF	Rovral® WG Fungicide
264-532	5/30/96	50% WP	Rovral® 50 SP
264-562 [3]	4/23/96	4 lb/gal SC/L	Iprodione HG Fungicide

[1] Including SLN Nos. AZ880001, CA850035, CA860064, CA880019, CA900013, OR810005, OR960011, WA810052, WA930026, WA930027, and WA940001.

[2] Including SLN Nos. AZ880001, OR960012, OR960032, WA940006, and WA960027.

[3] Homeowner label.

[Note: In addition to the EPs listed above, REFs identified the following SLN registrations with an unregistered parent product, DIVA® Fungicide: ID960011, MN960004, MO960002, and OR960033. These SLN registrations are classified to be FlC formulations with multiple active ingredients (1.5 lb/gal Iprodione + 3.0 lb/gal chlorothalonil) for use on potatoes. HED had no objection to the MO SLN.]

APPENDIX IV: RESIDUE CHEMISTRY SCIENCE ASSESSMENTS

Table D. Residue Chemistry Science Assessments for Reregistration of Iprodione.

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
860.1200: Directions for Use	N/A = Not Applicable	Yes [2]	See Table C
860.1300: Plant Metabolism	N/A	No	00086082 [3], 00137211 [4], 00162216 [5], 00166217 [5], **92083025, 92083026, 92083027, 92083074**
860.1300: Livestock Metabolism	N/A	No [6]	00130833 [7], 00130835 [8], **92083028, 92083029**
860.1340: Residue Analytical Methods			
- Plant commodities	N/A	Yes [9]	**00086085, 00126577, 00129166, 00131442, 00144915, 00150019, 00152488, 00156397, 00164882, 41071601** 43034102 [10], 43397101 [11], 43526801 [12], **92083073**
- Livestock commodities	N/A	Yes [13]	42169305 [14], 42169306 [14], 43958202 [15]
860.1360: Multiresidue Methods	N/A	No	43397102 [16], 43397103 [16]
860.1380: Storage Stability Data	N/A		
- Plant commodities	N/A	No	**40897801**, 43273401 [17], 43702501 [18], **92083032**
- Livestock commodities	N/A	No	00125811 [19], **00131418, 92083031**
860.1500: Crop Field Trials			
Root and Tuber Vegetables Group			
- Carrots	5.0 [§180.399(a)]	No	00164882 [20], **92083039**

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
- Ginseng	2.0 (ginseng) [§180.399(a)] 4.0 (ginseng, dried) [§185.3750]	No	00160754 [21], **92083042**
- Potatoes	0.5 [§180.399(a)]	No	00156397 [22], **92083046, 92083067**
Bulb Vegetables (*Allium spp.*) Group			
- Garlic	0.1 [§180.399(a)]	No	00125387 [23], **92083041**
- Onions (dry bulb)	0.5 [§180.399(a)]	No	00144915 [24], **92083078**
Leafy Vegetables (except *Brassica* Vegetables) Group			
- Lettuce (head and leaf)	25.0 [§180.399(a)]	No	00125812 [25], 00129166 [25], 00131442 [25], 00163456 [26] **92083044, 92083053, 92083054**
Brassica (Cole) Vegetables Group			
- Broccoli	25.0 [§180.399(a)]	No	00152488 [27], **92083037**
- Chinese mustard	15.0 [§180.399(c)]	No	41192801 [28]
Legume Vegetables (Succulent or Dried) Group			
- Beans (dry and succulent)	2.0 [§180.399(a)]	No [29]	00126577 [30], 00144291 [30], 00147226 [30], 43222501 [30], 43245801 [30], 43255701 [30], 43295101 [30], **92083036**

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
Foliage of Legume Vegetables Group			
- Beans, forage and hay	90.0 [§180.399(a)]	No [29]	00126577 [30], 00144291 [30], 00147226 [30], 43222501 [30], 43245801 [30], 43255701 [30], 43295101 [30], **92083036**
Citrus Fruits (*Citrus* spp., *Fortunella* spp.) Group			
- Tangelos	3.0 [§180.31]	Not for Reregistration[31]	42726301 [32]
- Tangerines	3.0 [§180.31]	Not for Reregistration[31]	42726301 [32]
Stone Fruits Group			
- Apricots	20.0 [§180.399(a)]	No [33]	00122712 [34], **92083059**
- Cherries	20.0 [§180.399(a)]	No	00086084 [34], 00086086 [34], 00086087 [34], 00122712 [34], 40541001 [34], **92083048, 92083057, 92083058, 92083059, 92083060, 92083075, 92083076, 92083077**
- Nectarines	20.0 [§180.399(a)]	No	00122712 [34], 40637201 [34], **92083059, 92083061**
- Peaches	20.0 [§180.399(a)]	No	00086084 [34], 00086086 [34], 00086087 [34], 00122712 [34], 40637201 [34], 41885401 [35], 44020001 [36], **92083048, 92083057, 92083058, 92083059, 92083061, 92083075, 92083076, 92083077**
- Plums (fresh prunes)	20.0 [§180.399(a)]	No	00122712 [34], 40637201 [34], **92083059, 92083061**
Berries Group			
- Blueberries	15.0 [§180.399(a)]	No [29]	43222502 [30]

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
- Boysenberries	15.0 [§180.399(a)]	No	
- Caneberries	25.0 [§180.399(a)]	No	40244001 [37], **92083038**
- Currants	15.0 [§180.399(a)]	No [38]	
- Raspberries	15.0 [§180.399(a)]	No	43262501 [37]
Tree Nuts Group			
- Almonds	0.3 (nutmeat); 2.0 (hulls) [§180.399(a)]	No	00064840 [39], 00150019 [39], **92083049**
Cereal Grains Group			
- Rice, grain	10.0 [§180.399(a)]	No [34]	00162214 [5], 40199201 [5], 40489207 [5], **92083047, 92083056, 92083065**
Forage, Fodder, and Straw of Cereal Grains Group			
- Rice, straw	20.0 [§180.399(a)]	No [34]	40489207 [5], **92083056**
Miscellaneous Commodities			
- Cotton, seed, and gin byproducts	0.10 (cottonseed) [§180.399(d)(1)]	Not for Reregistration[31]	41905801 [40], 43397101 [11], 43454001 [41], 43560701 [11]
- Grapes	60.0 [§180.399(a)]	No	00118392 [42], 00130836 [42], 00132747 [42], 41071601 [43], 42437101 [44], 43034101 [10], **92083043, 92083052, 92083066**
- Kiwifruit	10.0 [§180.399(a)]	No [29]	42132801 [45], 42506601 [46]
- Peanuts, nutmeat and hay	0.5 (peanuts); 7.0 (hulls); 150.0 (forage and hay) [§180.399(a)]	No [29]	00143398 [47], 00145163 [47], **92083045, 92083055**

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
- Strawberries	15.0 [§180.399(a)]	No	40094901 [48], **92083068**
860.1520: Processed Food/Feed			
- Cottonseed	None established	Not for Reregistration[31]	41905802 [40]
- Grapes	300 (raisins) [§185.3750]; 225.0 (grape, pomace, dry); 300.0 (raisin waste) [§186.3750]	No [43]	00118392 [42], 00130836 [42], 00132747 [42], **92083043**, **92083066**
- Peanuts	10.0 (soapstock) [§186.3750]	No	00145163 [47], **92083045**
- Plums	20.0 (prunes) [§180.399(a)]	No	43255702 [49]
- Potatoes	None established	No	40060201 [22], 40659601 [22], **92083046**, **92083067**
- Rice	30.0 (rice bran); 50.0 (rice hulls) [§186.3750]	No [34]	00162214 [5], **92083047**, **92083065**
860.1480: Meat, Milk, Poultry, Eggs			
- Milk and the Fat, Meat, and Meat Byproducts of Cattle, Goats, Hogs, Horses, and Sheep	0.5 (milk, fat, meat, and meat byproducts except kidney and liver); 3.0 (kidney and liver) [§180.399(b)]	No	00106082 [8], **92083035**
- Eggs and the Fat, Meat, and Meat Byproducts of Poultry	1.0 (meat); 1.5 (eggs); 3.5 (fat); and 5.0 (liver)	No	00130834 [50], 43958201 [15], **92083034**
860.1400: Water, Fish, and Irrigated Crops	None established	Yes [51]	

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
860.1460: Food Handling	None established	N/A	
860.1850: Confined Rotational Crops	N/A	Yes [52]	43596201 [53]
860.1900: Field Rotational Crops	None established	Yes [54]	00129166 [25], 00137231 [25], 43718201 [55]

Table D (continued).

1. **Bolded** references were evaluated as candidates for Phase 5 review in the Iprodione Phase 4 Review (C. Olinger, 3/15/91). All other references were reviewed as noted.

2. Provided that label amendments for ALL Iprodione end-use products are made for the following primary crops, no additional field residue data will be required:

   For beans, labels should specifically exclude cowpeas; with such restrictions, field residue data and tolerances for cowpea forage and hay will not be required (Memo, 8/12/96, J. Abbotts).

   For blueberries, labels should be modified to list blueberries and/or currants separately from caneberries (CBRS 13730 et al., 1/27/95, S.A. Knizner).

   For kiwifruit, labels for Rovral Flo and Rovral WP which allow use on kiwifruit grown in New Zealand should be modified to clearly state that the maximum application rate is 0.688 lb ai/A/application (or 0.75 kg ai/ha/application). For both labels, the recommended rate for kiwifruit corresponds to the minimum rate to be used for all crops on the label. The wording of the labels should be revised to indicate that the recommended rate for kiwifruit represents the **maximum** allowable application rate. If label revisions are not made to more clearly describe that the maximum Iprodione application rate for kiwifruit is 0.688 lb ai/A/application (or 0.75 kg ai/ha/application), then over-tolerance residues in/on kiwifruit may result.

   For peanuts, labels should be modified to prohibit the feeding of peanut hay to livestock (Memo, 8/12/96, J. Abbotts).

   For stone fruits, labels should reflect the risk reduction measures of March 1996: Elimination of post-harvest applications, reduction in the maximum number of applications per season from 5 to 4 (each at a maximum rate of 1 lb ai/A), and an increase in PHI from 0 to 7 days (CBRS No. 17768, 2/12/97, J. Abbotts).

   Provided labels meet the conditions set forth in PR Notice 93-2, the requirements for crop field trials reflecting aerial application of Iprodione on almonds, dry beans, and dry bulb onions are waived (CB No. 14300, DP Barcode D207150, 10/4/94, S. Knizner). For aerial applications of Iprodione to dry beans and dry bulb onions, the various end-use products must be diluted in a minimum of 10 gallons of water per acre, and for aerial applications to almonds, the products must be diluted in a minimum of 15 gallons of water per acre.

3. PP#2F2596; memo of 5/13/82, R. Perfetti.
   See also Phase 5 review (memo of 6/26/96, J. Abbotts).

4. PP#4G3037; memo of 5/31/84, N. Dodd.
   See also Phase 5 review (memo of 6/26/96, J. Abbotts).

5. PP#6F3443; CB No. 1326 and 1327, 5/17/87 and 4/25/88, R. Cook.
   See also Phase 5 review (memo of 6/26/96, J. Abbotts).

6. CBRS No. 17751, D233013, 2/4/97, J. Abbotts: An additional ruminant metabolism study will not be required provided that all applicable Iprodione end-use product labels prohibit use on cowpeas and prohibit the feeding of Iprodione-treated peanut hay to livestock animals, and that the 1x feeding level (theoretical maximum dietary intake) based on tolerances for feed items does not significantly increase above 30 ppm. If any registrant desires to support use on cowpeas or the feeding of peanut hay, or if new uses would significantly increase the 1x feeding level above 30 ppm, then a new ruminant metabolism study would be required to identify residues of concern and to generate samples for radiovalidation of an enforcement analytical method. An additional poultry metabolism study is not required.

7. PP#3F2964; memo of 2/21/84, R. Cook.
   CB No. 17751, DP Barcode D233013, 2/4/97, J. Abbotts.

Table D *(continued)*.

8. PP#2F2728; memo of 10/25/82, M. Kovacs.
CBRS No. 17751, DP Barcode D233013, 2/4/97, J. Abbotts.
CBRS No. 17802, DP Barcode D234162, 3/12/97, J. Abbotts.

9. CBRS 17749, D232981, 1/31/97, J. Abbotts: The potential for substituting a different solvent for benzene in registrant Method 151 remains an unresolved issue from Iprodione Phase 4 review. For each step in Method 151 where benzene is used, the registrant should describe the results of using a different solvent instead; if the use of benzene is preferable, then the registrant should explain why. The registrant should also explain why Method 151 is preferable to Method I in PAM, Vol. II, since the latter method does not use benzene.

10. CB No. 13135, DP Barcode D198251, 9/29/94, S. Knizner.

11. PP#2F04111; CB No. 14677, DP Barcode D209023, 2/6/95, G. Herndon.
CB No. 15214, DP Barcode D212723, 8/10/95, N. Dodd.

12. CBRS No. 15116, DP Barcode D211914, 12/12/95, S. Knizner.
CBRS No. 16620, DP Barcode D221630, 12/18/95, S. Knizner.

13. CBRS No. 17594, D230127, 2/6/97, J. Abbotts: Morse Laboratories SOP Method-71 should be amended in accordance with the recommendations of the laboratory that conducted the independent laboratory validation. Because Method-71 uses benzene as a reagent, the registrant should justify the use of this substance, including an explanation of how substitution of a different solvent affects results.

The registrant should additionally provide independent laboratory validation data for the proposed method for determining hydroxylated Iprodione residues (e.g., RP-36114) in ruminant milk and tissues. Consistent with Iprodione Phase 4 Review, the registrant should explain why use of benzene and diazomethane as reagents is necessary.

Finally, the registrant should provide and/or develop confirmatory method(s) for the determination of major Iprodione residues (parent Iprodione and metabolites RP-32490 and RP-36114) in livestock commodities. This requirement is based on the fact that the proposed methods are each converted to common moieties of dichloroaniline; therefore, there is a concern for interference from other pesticides. If such confirmatory method(s) can be successfully developed and independently validated, then CBRS will submit them directly for Agency validation, rather than either of the common moiety methods proposed for livestock commodities. CBRS recognizes that the registrant may have conducted additional method development work that has not been reported, and would be willing to consider alternative registrant proposals for meeting the data requirements for livestock enforcement analytical method.

14. CB Nos. 9664 and 9665; DP Barcodes D175846 and D175865, 5/29/92, L. Cheng.

15. CB No. 17594, DP Barcode D230127, 2/6/97, J. Abbotts.

16. Forwarded by CBTS to FDA (B. McMahon) for review (G. Herndon, 1/26/95).

17. CB No. 14162, DP Barcode D206161, 12/27/94, S. Knizner.

18. CB No. 16561, DP Barcode D220978, 4/17/96, J. Abbotts.

19. PP#2F2728; memo of 10/25/82, M. Kovacs.
CBRS No. 17802, D234162, 3/12/97, J. Abbotts.

20. PP#7E3474; CB No. 1631, 4/6/87, V. Boyd.
See additional review (memo of 8/12/96, J. Abbotts).

Table D (continued).

21. PP=6E3426 FAP=6H5504; CB Nos. 1191 and 1194, 9/23/86, R. Cook.
CB No. 17155, DP Barcode D225494, 5/2/96, B. Schneider.
See additional reviews (memo of 5/22/96 and 8/12/96, J. Abbotts).

22. PP=6F3366; CB Nos. 2226 and 2227, 8/4/87, R. Cook.
CB Nos. 4016 and 4017, 9/9/88, R. Cook.
See additional review (memo of 8/12/96, J. Abbotts).

23. PP#3F2841; memo of 7/1/83, K. Arne.
See additional review (memo of 8/12/96, J. Abbotts).

24. PP#4F3111; CB No. 775, 5/15/85, E. Haeberer.
See additional review (memo of 8/12/96, J. Abbotts).

25. PP#3F2840; memo of 11/21/83, K. Arne.
See additional review (memo of 8/12/96, J. Abbotts).

26. PP#7F3481, CB No. 1754, 4/8/87, M. Nelson.
See additional review (memo of 8/12/96, J. Abbotts).

27. PP#6F3305; CB No. 9, 12/5/85, W. Chin.
See additional review (memo of 8/12/96, J. Abbotts).

28. PP#9E3790; CB No. 5693, 11/28/89, F. Toghrol.

29. Pending required label amendments (see Endnote 2), the Reregistration requirements for this guideline topic will be considered fulfilled.

30. CB Nos. 13730, 13960, 13959, 14134, and 14496; DP Barcodes D203334, D204980, D205004, D206123, and D208275, 1/27/95; S. Knizner.
See additional review (memo of 8/12/96, J. Abbotts).

31. Data requirements for use of Iprodione on tangelos, tangerines, and cottonseed are not addressed in this document since they will be considered in future registration actions.

32. PP#3G4210.

33. [Deleted during editing.]

34. PP#2F2596; memo of 5/13/82, R. Perfetti.
PP#3F2810; memo of 3/21/83, R. Perfetti.
PP#8E3645; CB No. 3946, 7/22/88. R. Cook.
CBRS 17768, 2/12/97, J. Abbotts.

35. Memo of 3/7/96, J. Abbotts.

36. CB No. 17266, DP Barcode D226786, 6/28/96, J. Abbotts.

37. CB Nos. 13955 and 14497; DP Barcodes D205015 and D208276, 1/24/95, S. Knizner.
See additional review (memo of 8/12/96, J. Abbotts).

38. Data on blueberries, as representative of bushberries, can be translated to currants.

39. PP#5F3241; CB No. 962, 6/26/85, M. Firestone.
See additional review (memo of 8/12/96, J. Abbotts).

Table D (continued)

40. PP=1G3998: CB No. 8142, DP Barcode D165525, 6/8/92, J. Garbus.

41. CB No. 14991, DP Barcode D210829, 2/9/95, G. Herndon.

42. PP#3F2964/FAP#4H5415; memo of 2/21/84, R. Cook.
PP#3G2787; memo of 3/21/83, N. Dodd.
Memo of 5/6/96, J. Abbotts.

43. PP#4F4316; CB No. 13863, DP Barcode D204278, 8/1/94, S. Knizner.
CB No. 14402, DP Barcode D207412, 12/27/94, S. Knizner.
Memo of 5/6/96, J. Abbotts.
CB Nos. 17212 and 17213, DP Barcodes D226305 and D225989, 7/1/96, J. Abbotts.
CBRS 17786, D233617, 2/21/97, J. Abbotts.

44. CB No. 10507, DP Barcode D182097, 10/15/92, S. Knizner.

45. CB No. 9165, DP Barcode D172676, S. Funk, 6/9/92.
See also CB No. 14222, DP Barcode D206574, 10/4/94, S. Knizner.

46. CB No. 10807, DP Barcode D184060, 1/27/94, B. Cropp-Kohlligian.
See also CB No. 14222, DP Barcode D206574, 10/4/94, S. Knizner.

47. PP#4G3037; memo of 5/31/84, N. Dodd.
PP#4F3129, CB. Nos. 225 and 226, 2/15/85, R. Cook.
See additional review (memo of 8/12/96, J. Abbotts).

48. PP#7F3510; CB No. 2261, 5/15/87, M. Nelson.
See additional review (memo of 8/12/96, J. Abbotts).

49. CB No. 13956, DP Barcode D205006, 1/24/95, S. Knizner.
CBRS 17768, D233289, 2/12/97, J. Abbotts.

50. PP#3F2964; memo of 2/21/84, R. Cook.

51. Phase 4 Review: Data are required on residues in water as a result of use on rice. Provided the label restriction against aquiculture in treated rice fields remains, data on fish are not required.

52. The registrant should supply additional information concerning the characterization and identification of radioactive residues in/on rotational crop matrices. Specifically, the registrant should resolve the issues raised in Conclusion 11 of the subject CBRS review (Endnote 53).

53. CB No. 15422, DP Barcode D214277, 6/9/95, S. Knizner.

54. Determination of the nature of the residue in confined rotational crops and a decision by the HED Metabolism Committee on the residues to be regulated in rotational crops are necessary before the Agency can advise the registrant on the residue data required for extensive field trials.

55. CB No. 16553, DP Barcode D220980, 4/17/96, J. Abbotts.

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Chemical:	**Iprodione (ANSI)**
PC Code:	**109801**
HED File Code	**14000 Risk Reviews**
Memo Date:	**07/31/1998**
File ID:	**TX012696**
Accession Number:	**412-01-0082**

HED Records Reference Center
01/10/2001